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THE EVOLUTION OF THE THYROID GLAND.

By David Marine, M. D.

(From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University,[1] Cleveland.)

The thyroid while it does not play an essential rôle in our conception of vertebrates is, nevertheless, one of their most constant and characteristic structures—existing in the same anatomical form from the adult cyclostomes (Petromyzon and Bdellostoma) throughout all the fishes, amphibians, reptiles, birds and mammals.

In the larval Petromyzon—Ammocœtes branchialis—in Amphioxus and in all Tunicates there exists in the ventral midline of the branchial sac a gland-like structure which Huxley[2] first designated as "Endostyle." This endostyle or better, endostylar mechanism[3] has, through the work of Goodsir, been shown to have the same general structure in both the Tunicates and Amphioxus, and Wilhelm Müller (Jenaische Zeitschrift, 1873, VII, 327), in 1873, pointed out the similarity of the structure in Ammocœtes with that of the Tunicates and Amphioxus and suggested that the endostyle of the lower chordates was homologous with the ductless thyroid of the higher chordates. This homology has been strengthened by the subsequent work of Anton Schneider (Thyroidea von Ammocœtes, Beiträge z. Vergleich. Anat. u. Entwcklngs-

[1] The observations on the Tunicates and Amphioxus were made at the Marine Biological Station at San Diego during the summer of 1911. I am indebted to Dr. W. E. Ritter, Director, for the privileges and excellent facilities of his laboratory. The work with Ammocœtes was done in the Laboratory of Histology and Embryology, of Cornell University, during the summer of 1912. I wish to thank Dr. B. F. Kingsbury for the privileges of his laboratory and many helpful suggestions and criticisms.

[2] Huxley (Observations on Salpa, Pyrosoma, Doliolum, etc., Philos. Trans., 1851, 566) appears to have first introduced the term "Endostyle." He so named it from his belief that this prominent fold in the Tunicates branchial sac was rod-like and served as a brace for the delicate branchial sac. Later work showed it to be a groove lined with highly differentiated gland cells. In German literature it is usually spoken of as the "Hypobranchial Groove." At present both terms are in common use for the structure in both the Tunicates and Amphioxus. When a similar structure in Ammocœtes was found to give rise to the ductless thyroid follicles at metamorphosis the term "Thyroid" was introduced and is now quite generally applied to the endostyle of Ammocœtes. Inasmuch as it has no resemblance to a true thyroid and is entirely similar to the endostyle of the Tunicates and Amphioxus I will use the term "Thyroid" only in connection with the ductless follicle formations.

[3] In Tunicates in addition to the glandular portion of the endostyle or hypobranchial groove there are two anterior peripharyngeal ciliated bands which begin at the anterior end of the glandular portion of the endostyle, arch around the anterior end of the branchial sac—one on each side—to join in the dorsal midline in the ciliated dorsal ridge or lamina which extends directly posterior to the entrance into the œsophagus. At the posterior end of the hypobranchial groove the marginal folds form two slight ridges which have been traced around the posterior end of the branchial sac to join the dorsal lamina near its termination in the œsophagus.

In Amphioxus the two peripharyngeal grooves also start from the anterior termination of the glandular portion of the endostyle and arch around the anterior border of the branchial sac to meet

gesch. der Wirbelthiere, Berlin, 1879, 85) and Anton Dohrn (Die Thyroidea bei Petromyzon, Amphioxus und den Tunikaten, Mittheil. Zool. Stat., Neapel, 1886, VI, 49) and is as firmly founded as morphological studies make possible. Below the chordates nothing comparable to an endostylar structure has been made out and even in the lowest class of chordates—Balanoglossus—the structure is absent. Ritter (On a new Balanoglossus larva from the coast of California and its possession of an endostyle, Zool. Anz., 1894, XVII, 24) has described a ridge or band of high ciliated epithelium in the midline of the œsophagus of a Tornaria (larval Balanoglossus) which, from its location and from the generally accepted systemic position of Balanoglossus he suggested might be homologous with the Tunicates endostyle. Morgan (The Development of Balanoglossus, Jour. of Morph., 1894, IX, 1) also described this structure but did not use it as evidence of this animal's possible relation to the true chordates. While I was working in Dr. Ritter's laboratory during the summer of 1911 the question of the relation of this oro-œsophageal mechanism of Tornaria to the Tunicate endostyle was discussed with him and he expressed the opinion that the evidence was insufficient for assuming any phylogenetic relationship.

Leaving out Balanoglossus as doubtful possibly as regards its systemic position as a chordate and certainly as regards the endostylar nature of the oro-œsophageal, ciliated, gland cell mechanism, the lowest undoubted and living relative of the thyroid mechanism is found in the Tunicates.[4]

More than a thousand species of Tunicates have been described (Ritter, W. E.: Am. Naturalist, 1907, XLI, 453). The several groups present great variations in external appearance (sessile, pellagic, simple, colonial) although their internal structure is strikingly constant. The endostylar mechanism is a good example of this constancy of organs and it rarely presents variations in morphology sufficient to be of value in the differentiation of species (Herdman: Liverpool Marine Biol. Mem., 1899, XI, No. 1, 14).

The large simple Ascidian Holocynthia johnsonii, is very common in San Diego Bay and most of my observations were made on this species, although through the courtesy of Dr. Ritter I made microscopic preparations from many of his general collection of Tunicates including several species of Salpa, Pyrosoma, Ciona, Cynthia, Doliolum and Appendicularia.

in the dorsal midline in the dorsal groove (a ridge in Tunicates) which extends back to the entrance to the œsophagus.

In Ammocœtes the grooves are more prominent owing to the fact that the glandular portion of the endostyle is largely cut off from the pharynx and opens into it by a large duct-like elliptical opening. Beginning at the anterior lip of this duct and continuous with it is a correspondingly large, deep, ciliated groove (T-shaped in cross-section) which after extending a short distance anteriorly branches into right and left ciliated peripharyngeal grooves which arch around the anterior end of the pharynx to join the prominent midline dorsal ridge where they fuse with the ciliated epithelium on the sides of this pendant-like fold and continue back to the œsophagus. The ventral or most dependent portion of this fold is covered with stratified squamous epithelium out of which the permanent œsophagus will be formed. Beginning at the posterior lip of the endostyle duct and continuous with it is a midline, shallow, ciliated groove which extends back to the entrance to the larval œsophagus.

[4] The endostyle-thyroid mechanism has been utilized in the philosophical discussions of the origin of vertebrates. Whether the primitive Tunicate which Brooks (The Genus Salpa—Johns Hopkins Press, Baltimore, 1893) believed was typified in all essentials in the existing *Appendicularia* arose in the main stem of the descent of chordates or whether all Tunicates are degenerate forms of fish-like ancestors unrelated to the vertebrate tree, as Dohrn and others believe, is a question that does not concern us here. The data of the endostyle-thyroid mechanism can only be a minor item in such a controversy, but so far as they can be utilized in the elaboration of any hypothesis of the origin of vertebrates it seems that the views of Brooks more nearly harmonize these facts of structure, function and historical sequence than do the views of Dohrn, Gaskell, Patten and others which would leave the origin of the endostyle unexplained. Brooks (Origin of the Thyroid, Johns Hopkins Hosp. Bull., 1893, IV, 47) considered the endostyle of the Tunicate to have arisen with the branchial sac as a specialization to meet the needs of its habits and modes of life.

Tunicates.

(Fig. 1, Plate III, and Fig. 2.)

The glandular portion of the endostylar mechanism forms a groove (roughly U-shaped in cross-section) lying in the ventral midline of the pharyngeal or branchial sac. This groove begins near the anterior end of the pharynx just posterior to the oral tentacles, at the ventral junction of the peripharyngeal ciliated bands and extends backward nearly to the œsophagus. In all the larger Tunicates it is visible to the naked eye as a prominent, whitish, longitudinal fold embedded in the wall of the branchial sac. The groove opens throughout its length into the branchial sac but owing to the elasticity of the branchial sac and the muscular mantle the mechanism exists for closing the groove by apposing its lateral walls.

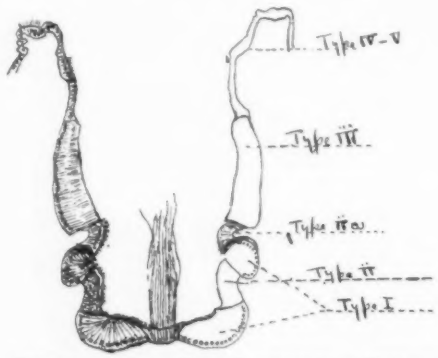

Fig. 2.—Diagrammatic outline of endostyle of Holocynthia johnsonii as seen in cross-section.

Histologically the groove is lined with highly differentiated gland cells. When seen in cross-section there is in the ventral midline of the groove a tract composed of closely packed columnar cells with deeply staining nuclei bearing whiplike cilia whose lengths in many species nearly equal the depth of the groove. On either side of this unpaired tract of ciliated

cells the fundus, lateral wall and marginal fold of the groove contain symmetrical epithelial formations. These symmetrical epithelial tracts form the basis of homology with the endostyle of Amphioxus and Ammocœtes. There are at least four and possibly five types of epithelia. The most uniformly constant type in form and position comprises two large tracts of cuneiform gland cells in each half of the endostyle which I will call Type I. These wedge-shaped cells of each tract are arranged radially from the common point of opening into the endostylar groove and each bundle is roughly fan-shaped. The more ventral bundle is usually slightly larger. The cells are pale, granular, with large vesicular nuclei lying at the bases of the cells (periphery of the bundle). These two bundles of Type I cells in each half are separated by an intervening layer of short, closely packed, columnar, ciliated cells with deeply staining nuclei lying in different levels of the cell bodies which may be designated as Type II. The height and extent of these cells vary with different species being as a rule more extensive in the Salpae. Just above the upper bundles of cuneiform cells (Type I) and closely applied to them is another short area of cells, columnar and ciliated in Ascidians and cuboidal in Salpæ, which differ from the cells of Type II. For convenience these may be spoken of as Type II-A. Above this somewhat variable layer of Type II-A cells is a very long area in each half of large, high, columnar cells that may be designated as Type III. These cells are not ciliated in any of the species examined. Above this group in each half and continuing to the marginal fold or lips of the groove is another group which I shall designate as Types IV and V. These cells are in general cuboidal, often containing yellow pigment granules, and non-ciliated although, just at the margin of the fold and its junction with the branchial mucosa, there is on each side a small area of ciliated, low, columnar cells with deeply staining nuclei.

Summing up then, the endostylar groove proper is lined with highly differentiated epithelium which may be divided into at least four and possibly five different types in addition to the unpaired midline epithelium.

AMPHIOXUS LANCEOLATUS.

(FIG. 3, PLATE III, AND FIG. 4.)

The glandular portion of the endostyle in the adult Amphioxus forms a broad shallow groove situated in the ventral midline of the pharynx and extending practically the whole length of the pharynx terminating anteriorly in the peripharyngeal ciliated bands and posteriorly just anterior to the œsophagus. The groove opens into the branchial sac throughout its length and it does not appear that the groove can be closed off from the pharynx as it can be in the Tunicates.

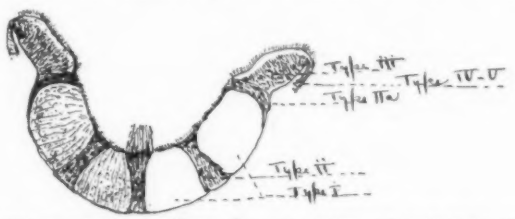

FIG. 4.—Diagrammatic outline of cross-section of endostyle of Amphioxus calif.

Histologically as Goodsir, Müller, Schneider, Dohrn and many others have shown it is composed of the same basic types of epithelium already described for the Tunicates. Seen in cross-section there is in the ventral midline of the endostyle a small bundle of tall, columnar, deeply staining cells with long upright cilia. On either side of this unpaired tract are two bundles of large, pale, columnar, slightly wedge-shaped cells, which, on account of their resemblance to Type I of the Tunicates, may also be designated as Type I. They differ from the corresponding cells of the Tunicates in that they are tipped with short cilia-like processes. Between the two bundles of cells of Type I on either side is a very narrow layer of columnar ciliated cells with deeply staining nuclei which from their location and staining characteristics are similar to Type II of the Tunicates and may here be designated as Type II. Just above and closely applied to the upper bundle of cuneiform cells of Type I on each side is a very narrow zone of cells which, as regards size, shape and staining reaction, are almost identical with Type II and I have designated them Type II-A since they correspond in position to the group of cells designated Type II-A for the Tunicates. Beyond or above the cells of Type II-A and producing the marginal fold are long areas of high columnar, ciliated, closely packed cells with deeply staining nuclei which, as regards extent and location, closely resemble the Type III for the Tunicate endostyle except that they are ciliated and may also be designated as Type III for the Amphioxus. Above the cells of Type III and curving sharply externally and ventrally and fusing with the branchial mucosa in the ventral-lateral sulcus of the pharynx is a poorly defined layer of low cuboidal epithelium which is analogous with Types IV and V of the Tunicates in position and structure and may also be designated Types IV and V.

To sum up then, the endostylar groove proper is lined by highly differentiated epithelia of at least four different types in addition to the median, unpaired, ciliated tract and is similar in all its general characteristics to the endostyle of Tunicates. There are some differences. Thus the groove in Amphioxus is more compact, shallower and relatively wider than in Tunicates. Only three of the types of epithelium are contained in the groove proper in Amphioxus and all these cells are ciliated and of quite uniform height. These differences are but modifications as the fundamental structures correspond with those of the Tunicates.

AMMOCŒTES BRANCHIALIS.

(FIGS. 5 AND 6, PLATE III.)

The fully developed endostylar groove shows many modifications of the form seen in the Tunicates and Amphioxus. Thus the glandular portion is shut off from the pharynx except for the large elliptical duct-like orifice, and the pharyngeal grooves anteriorly and posteriorly are correspondingly

increased. Embryologically it has been shown (Reese, A. M.: Proc. Am. Acad. Nat. Sci., Phila., 1902, 85) that at first the endostyle is an open ventral midline groove in the floor of the branchial sac just as in Tunicates and Amphioxus but in the course of its development great distortions and modifications are required.

The glandular portion of the endostyle is divided into symmetrical right and left halves by the median septum and each half contains the same complement of epithelia that is present in the whole endostyle of the Tunicates or Amphioxus, or in other words—the fully developed endostyle of Ammocœtes is similar to two simple endostyles placed side by side. In cross-section of a half of the endostyle one notes the absence of the tract of cells which in Tunicates and Amphioxus bears the long whiplike cilia as well as of any tract of cells that may be homologized with them. The next group of cells consists of the four tracts—two on each side of the midline of each half—of large cuneiform cells which in shape, size and staining reactions are identical with Type I of the Amphioxus and Tunicate endostyle. These cells formed the basis for the first homology by Müller. On each side of the openings of these bundles of wedge-shaped cells are areas of columnar, ciliated, closely set cells with deeply staining nuclei that may be designated as Type II since they correspond in location and type to the Type II of Amphioxus and Tunicates. Closely applied to one border of the cells of Type II is another group of larger, columnar, ciliated cells with large vesicular nuclei and containing yellow pigment granules which I have designated Type III. In the Tunicate endostyle the yellow pigment is commonly present in the cells which have been grouped under Types IV and V. It may be, therefore, that the epithelium grouped as Type III in the Ammocœtes endostyle is actually homologous with Types IV and V of Tunicates rather than with the epithelium I have grouped as Type III. Beyond Type III, covering the apex of the visceral invagination and the baso-lateral angles and continuous with the epithelium lining the duct and pharyngeal groove, is another type which in Ammocœtes I have grouped separately as Type IV. As will be seen later this Type IV is the most important epithelium concerned in the formation of the ductless thyroid follicles at metamorphosis. Type IV merges into another form which lines the parietal wall of the chamber and is designated as Type V. The cells of this type are flat, almost endothelial in form.

The metamorphosis (Fig. 7, Plate III) of Ammocœtes into Petromyzon which was first made known in 1856 by A. Müller gives us the great connecting link in the evolution of the thyroid mechanism, without which the relation of the endostyle to the thyroid could not have been known. The occurrence of a living animal which in its larval form has an endostyle only and in its adult form a ductless thyroid only allows one to observe the formation of typical ductless thyroid follicles out of the fullest development of the endostyle. Only the endostyle of larval Cyclostomes undergoes this metamorphosis. The metamorphosis from its beginning to its completion in Ammocœtes extends over a period of at least a month. The endostylar changes are at first a general shrinkage in all the component parts of the organ. The changes of greatest significance are those of the epithelia. The first to disappear are the tracts of large cuneiform cells (Type I) which are the most characteristic cell groups in the endostyle. The cells of Type III stand next to those of Type I in point of the rapidity of the cell atrophy and absorption although remnants of this type (easily identified by means of the yellow pigment) can be seen after the ductless follicles are formed. The flattened epithelial cells of Type V show the next most extensive changes although here also atrophic and distorted cell masses may be preserved until ductless follicle formation is nearing completion. It seems certain that the cells of Types I, III and V take no part in the ductless follicle formation. With the Types II and IV one cannot be certain that both do not take part although Type IV is certainly the most important epithelium persisting as the lining epithelium of the permanent follicles. The fact that Type IV is the predominant persistent epithelium of the ductless follicles and also that it is continuous with and probably identical with that epithelium lining the gland duct and the ventral pharyngeal grooves seems to me of the greatest significance in the interpretation of the origin of the thyroid of higher vertebrates. This observation, taken in connection with the observations of Dohrn that in the torpedo embryo transient rudimentary pharyngeal grooves are present, is strong evidence that the ductless thyroid of higher vertebrates originates from a pharyngeal anlage closely related to if not homologous with the epithelium which lines the pharyngeal groove and duct of the Ammocœtes endostyle.

The ductless thyroid follicle of the type present in Petromyzon persists throughout all the remaining classes of vertebrates in the same anatomical form and this allows some conception of the vast antiquity of the gland. In none of the chordates above the larval Cyclostomes is there a true endostyle formation. Dohrn and others have shown that a transient and rudimentary formation of the pharyngeal grooves can be made out in the very early stages of development of the lower rays and sharks but even this remnant of the endostylar mechanism cannot be traced into the higher vertebrates.

Beginning with the fishes and continuing throughout the remaining vertebrates the problem of the evolution of the thyroid is the problem of the embryology, which is still unsettled as regards mammals. In fishes the thyroid resembles very closely that of Petromyzon in position, arrangement of follicles, and as a rule (excepting elasmobranchii) in the absence of a capsule. The gland in fishes arises from a single median ventral anlage of entoderm in the region of the first gill arch.

In amphibians the adult thyroid is paired. Each body is surrounded by a fibrous capsule. Embryologically the gland arises from a single median ventral anlage of entoderm in the region of the first gill arch. This anlage grows downward and backward and divides into right and left halves which in the adult frog come to lie on the ventral surface of the posterior horns of the hyoid bones (Mayer: Zur Lehre von der

Schilddrüse und Thymus bei den Amphibien, Anat. Anz., 1888, III, 97).

In reptiles the adult thyroid is unpaired in the snakes (ophidia) and turtles (chelonia) and paired in the other groups (lizards, crocodiles, etc.) and lies in the thoracic cavity just above the pericardium. Embryologically all observers are in agreement that it arises from a single median ventral anlage in the region of the first gill arch and is shifted backward with the aortic arteries.

In birds the thyroid lobes are separate, oval bodies placed on each side of the vertebral column a short distance above the pericardium and usually partially imbedded in the lowermost lobules of the thymus. Embryologically the first accurate description was given by Remak in 1855 who derived the gland from an unpaired median ventral anlage of pharyngeal entoderm in the region of the first gill arch. He observed that as development proceeded it divided into a T-shaped process and shifted backward with the aortic arches to occupy an intra-thoracic position. The thyreo-glossal tract and isthmus were absorbed. These observations were accepted (by Gotte, Müller and Seessel) until 1881 when Stieda and Wölfler stated that the thyroid had a lateral origin as well as a median. Mall, in 1887 (Archiv. f. Anat. u. Physiol., 1887, 1-34), working with the development of the chick thyroid came to the conclusion of Remak that the chick thyroid is derived wholly from the single median anlage in the region of the first gill arch. The derivatives of the fourth gill pouch Mall designated as "Körpern Y" and concluded that they had nothing to do with the thyroid. Subsequent work has established the original views of Remak, Müller and Mall, that the avian thyroid is derived solely from the single, median, ventral, pharyngeal anlage of the first aortic arch.

In mammals the question as to whether the thyroid arises from one or three anlagen is still argued although the evidence brought forward during the last ten years has apparently settled the controversy. In mammals only, therefore, is there at present any doubt as to the single and median origin of the thyroid. Many of the earlier observers including Wilhelm Müller (Jenaische Zeitschrift, 1871, VI, 428) believed the mammalian thyroid arose from the single median anlage. Although Remak in the chick, His and Kölliker in the rabbit, Wölfler and others had partially observed paired lateral bodies whose fate could not be decided but which some believed to be part of the thyroid tissue, it remained for Stieda, in 1881, working with sheep embryos, to give the first important description of these paired bodies from the fourth pouch and he called them "Lateral thyroid anlagen." He believed the whole thyroid was derived from these two lateral anlagen. In 1883 Born (Archiv. f. mikr. Anat., 1883, XXII, 271), working with pig embryos confirmed Stieda's discovery of the lateral thyroid anlagen, but showed that the median anlage formed thyroid tissue and fused with the two lateral anlagen thus deriving the thyroid from three separate anlagen. His in 1885 (Anatomie menschlicher Embryonen, Leipzig, 1885, Heft 3), working with human embryos also found these lateral thyroid anlagen arising from the fourth pouch and concluded that the median anlage formed the isthmus and pyramidal process of the thyroid while the lateral anlagen formed the lateral lobes. This view, while it prevailed for 20 years following 1885, was questioned by Kastschenko, in 1887 (Archiv. f. mikr. Anat., 1887, XXX, 1), who worked with the sheep embryo. He concluded that these lateral anlagen played no important rôle in the development of the thyroid. These same bodies in the chick Mall had designated "Körpern Y." Van Bemmelen, in 1889 (Anat. Anz., 1889, IV, 400), homologized the "Körpern Y" (Mall) of chicks, post-branchial bodies (Maurer) of amphibians and the lateral thyroid anlagen (Stieda, Born) of mammals with the superpericardial bodies (Van Bemmelen) of Selachians and Ganoids. The later work of Maurer (Die Schlundspaltenderivative von Echidna, Verhandl. d. Anat. Gesellsch., 1899, XIII, 88) of Hermann and Verdun (Compt. rend. Soc. Biol., 1900, LII, 933) have further established that the lateral thyroid anlagen or post-branchial bodies play no part in the development of the thyroid, that in the lower mammals (Monotremes and

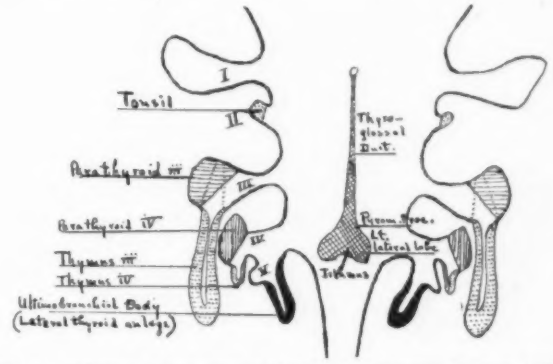

FIG. 8.—Schema of the branchiogenic derivatives in man (after Grosser in Keibel and Mall—Human Embryology, 1912, II, 461).

Marsupials) they tend to remain separate from the thyroid proper, although in the placental mammals they are as a rule imbedded in the posterior lateral portion of the lateral thyroid lobes. Fox (Am. Jour. Anat., 1908, VIII, 187) arrived at similar conclusions for the rabbit embryo. Grosser (Anat. Anz., 1910, XXXVII, 337) has summarized this trend in the views as to the fate of the lateral thyroid anlagen. He would abandon the term "Lateral Thyroid Anlagen" as a misnomer and would substitute the terms "Ultimobranchial" or "Telobranchial" body instead of post-branchial body (Maurer) or superpericardial body (Van Bemmelen) because it is believed that in the human embryo these bodies are derived from the rudimentary fifth pouch rather than from the fourth. (Fig. 8.)

With this short review of the embryological evidence that the mammalian thyroid is derived wholly from the median anlage I shall next review briefly the equally important evidence obtained from the developmental anomalies and the pathology all of which is associated with the median anlage. It has long been known that thyroid tissue in the form of a tract or as isolated masses was not of uncommon occurrence

along the path of descent of the original thyroid anlage, *i. e.* from the foramen cæcum to the thyroid isthmus (Merten: Archiv f. Anat. u. Physiol., Anat. Abth., 1879, 483). Streckeisen (Virchow's Archiv, 1886, CIII, 131 and 215), in a careful series of observations on the human thyroid, showed that the persistence of thyroid tissue along the thyreo-glossal tract was very common in districts where goitre was endemic and was always associated with a general thyroid enlargement which probably began during fœtal life. His (Archiv f. Anat. u. Physiol., Anat. Abth., 1891, 26) pointed out that in man the thyroid tract begins to atrophy normally during the fifth week of intra-uterine life. When abnormal demands for thyroid activity begin before this normal atrophy is completed a cell proliferation involving all the existing thyroid tissue takes place instead of the physiological resorption. The so-called sub-lingual, suprahyoid and infrahyoid thyroid masses as well as the pyramidal process are the commoner persistent forms of the thyreo-glossal tract. Thyreo-glossal cysts in which all thyroid tissue have disappeared are also relatively common in goitre districts. While much less studied, similar evidences of persistent remnants of the thyreo-glossal tract are present in the lower mammals. Wölfler has described such cases. I have also seen many instances in congenital goitre in dogs. Here the most common forms are the subhyoid accessory thyroids and the persistence of the thyroid isthmus. Goodey (Anat. Anz., 1910, XXXVI, 104) has described a persistent canal of His (thyreo-glossal duct) in a primitive selachian (Chlamydoselachus Anguineus).

In cases of aplasia of the thyroid Maresch (Zeitschr. f. Heilkunde, 1898, XIX, 249) and Erdheim (Zeigler's Beitr. z. Path. Anat. u. Allg. Path., 1904, XXXV, 366) have shown that the parathyroids are usually normal but that in the region of the fourth pouch parathyroid a cystic entodermal rest corresponding to the post-branchial or ultimo-branchial body or lateral thyroid anlage may usually be found although never any thyroid tissue. Getsowa (Virchow's Archiv, 1911, CCV, 208) working with the atrophic goitrous thyroids of cretins and idiots has observed these cell rests and cysts between the fourth pouch parathyroid and the lateral thyroid lobes. She noted that these rests did not react with the thyroid in developing goitre and considered them as ultimo-branchial bodies, which in mammals are functionless remnants or at least take no part in the formation of thyroid tissue.

All the evidence, therefore, from embryology, from congenital developmental defects, and from pathology is against the view that the post-branchial bodies or "Körpern Y" or lateral thyroid anlagen have any part in the formation of the thyroid gland. The different conclusions of the earlier observers were probably due in part at least to the fact that in mammals these bodies fused with the lateral thyroid lobes although in all lower vertebrates they remained separate and while functionless in mammals are believed to be active organs in sharks and possibly amphibians.

Physiology.

Concerning the function of the endostyle organ little is known. The observations and experiments of Giard (Arch. de Zool. Exper., 1872, I, 525 and 1873, II) and Fol (Morph. Jahrb., 1874, I, 222) on the transparent Synascidia, Salpa and Doliolum by means of India ink have shown that the endostyle is an active gland concerned in an important way with the collection of and possibly digestion of food. They observed that the gland cells secrete a slime or mucinous substance in which the food particles taken into the branchial sac with the respired water are caught up and that this mucin is formed into a cord by means of the cilia and carried forward to the peripharyngeal bands, thence along these ciliated tracts to the dorsal lamina and thence backward to the œsophagus. These observations have been confirmed by subsequent observers. All observers have suggested a possible chemical digestive action for this mucin but of this possibility nothing is known.

Reasoning from analogy the same function is believed to obtain in the Amphioxus and Ammocœtes endostyles. Alcock (Jour. Anat. and Physiol., 1899, XXXIII, 612), working under Gaskell, studied the digestive effects of extracts of various Ammocœtes tissues on fibrin. She was able to demonstrate a pepsin-like ferment in the liver, intestine and pharynx, but could obtain no evidence that the endostyle contained any proteolytic ferment.

In view of the important relation of iodin to the ductless thyroid I have made several iodin determinations on the tissues of Holocynthia johnsonii, on Salpa confederata and Amphioxus the averages of which are as follows:

	Mgm. of iodin per Gm. dried tissue.
Salpa confederata (whole animal)	Trace
Holocynthia johnsonii (whole animal except tunic)	0.03
" " tunic tissue	3.63
" " branchial sac tissue	0.00
" " endostyle tissue	0.00
" " dorsal lamina tissue	0.00
" " mantle (muscular tissue)	0.01
" " gut (with contents)	0.08
" " liver tissue	0.03
" " ova	0.01
Octopus—legs	0.00
Amphioxus lanceolatus (whole animal)	Trace

The results are wholly negative as regards the endostyle but one thing of interest, which so far as I have seen is not referred to, is the very high iodin content of the tunic of the Ascidians. The tunic contains much cellulose and the presence of iodin in it may be of the same significance as in ocean plant life generally.

As to Ammocœtes, I have kept them for nine months in an atmosphere of iodin to see whether the structure of the endostyle might be modified by it. The results were entirely negative. Iodin determinations were not made on the endostyle tissue either with or without administration of iodin. From these meager observations on the physiology of the endostyle one can state only what morphologists had already stated, that the function of the endostyle is probably quite different from that of the ductless thyroid. From its size and position at the beginning of the alimentary tract of all the three classes of animals possessing the endostyle and from its known mechanical action in the collection of food particles by

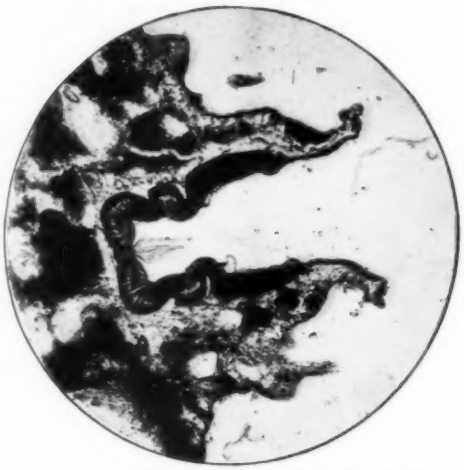

FIG. 1.—Photomicrograph of cross-section of endostyle of Holocynthia johnsonii with adjacent parts of branchial sac.

FIG. 3.—Photomicrograph of cross-section of endostyle of Amphioxus calif., showing relation to branchial sac and gill filaments.

FIG. 5.—Photomicrograph of endostyle of Ammocœtes branchialis as seen in cross-section at the level of the duct. One notes twice the epithelial complement of the simple endostyle of Amphioxus or Tunicates.

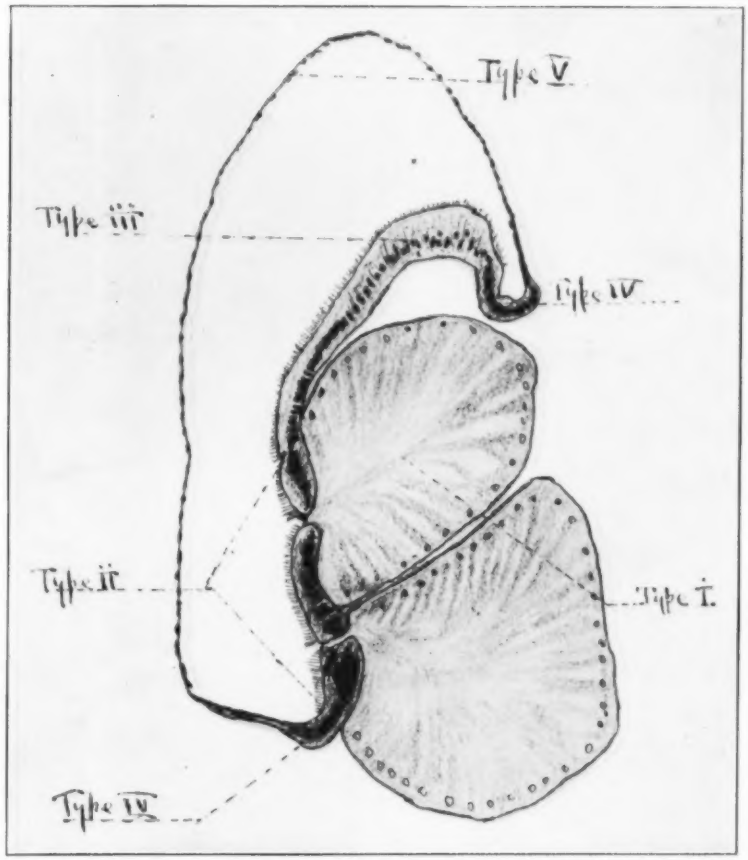

FIG. 6.—Camera outline of cross-section of the left external chamber of the endostyle of Ammocœtes posterior to the coiled inner chambers, *i. e.*, containing ¼ the epithelial investment of the whole endostyle or ½ the epithelial investment of the simple endostyle of Tunicates or Amphioxus.

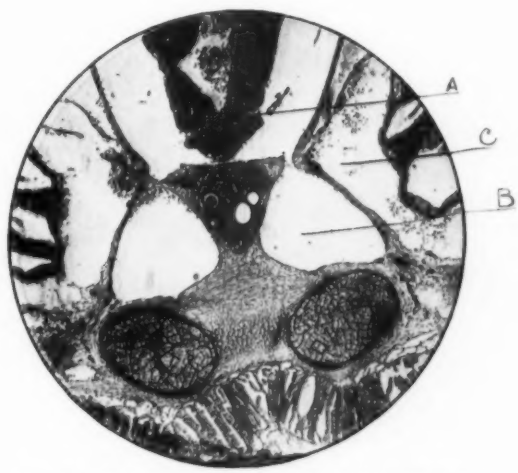

FIG. 7.—Photomicrograph of cross-section of thyroid area in a recently metamorphosed Ammocœtes branchialis showing relation of follicles to (A) tongue, (B) blood spaces, (C) gills.

means of its mucinous secretions it certainly subserves a function of prime importance in the nutrition of these animals.

SUMMARY.

Tunicates, Amphioxus and Ammocœtes are the only classes of animals which possess well developed endostyles. Goodsir, Müller, Schneider, Dohrn and all subsequent observers have shown that morphologically the endostyles are fundamentally identical in all. Cyclostomes, fishes, amphibians, reptiles, birds and mammals are the only classes of animals which possess ductless thyroids, the follicles of which are anatomically identical in all. The demonstration of the ontogenetic relationship between the endostylar mechanism and the true thyroid has been made possible through the preservation of a single class of chordates—the Cyclostomes—and the discovery by Schneider that during the metamorphosis of Ammocœtes into Petromyzon, typical ductless thyroid follicles are formed from the endostyle and as I have shown (Jour. Exp. Med., 1913, XVII, No. 4) out of one and possibly two persistent epithelia. The most important of the epithelia concerned in the formation of the ductless follicles is that form which is continuous with the lining epithelium of the duct and pharyngeal grooves. Additional data of this relationship are afforded by the observations of Dohrn that in some of the lower fishes a transient system of peripharyngeal grooves is present in the earlier stages of embryological development. This overlapping, so to speak, of the endostylar mechanism of the lowest chordates onto the ductless thyroid mechanism of the higher chordates is as firmly established as morphological studies make possible. Studies in the embryology of the ductless thyroid have shown that in fishes, amphibians, reptiles and birds the thyroid arises solely from a median, single, ventral downgrowth of the pharyngeal entoderm in or slightly anterior to the first aortic arch. In mammals this symmetry of development was believed to be departed from through the discovery by Stieda of the so-called "lateral thyroid anlagen" from the fourth or more accurately in man the rudimentary fifth gill pouch, but the work in the embryology, in the pathology and in the developmental defects of the thyroid during recent years has shown that these lateral bodies which in mammals only become imbedded in the lateral thyroid lobes take no part in the formation of thyroid gland tissue. This solution of the origin of the mammalian thyroid from the single median anlage harmonizes the location and development of the endostyle with the location and development of the ductless thyroid. The thyroid mechanism, therefore, irrespective of the possible phylogenetic relationship to the chordate stem of the several classes of animals concerned, appears to have been evolved through a direct line of descent from the Tunicates through the Amphioxus, fishes, amphibians, reptiles, birds and mammals. The meager evidence of the physiology in both the endostyle and the ductless thyroid gives no suggestion of an inter-relationship or function. Primarily the thyroid is a part of the alimentary tract and in its endostylar form is a digestive gland of great importance through its probable external secretion. In its ductless form it is only the atrophic remnant of its ancestor which, while it has suffered a corresponding distortion of function, still profoundly influences the animal's nutrition through the effect of its probable internal secretion.

HYPERSENSITIVENESS TO TUBERCULO-PROTEIN AND TO TUBERCULIN.*

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Few problems in experimental medicine have stimulated so much work, or have given rise to so large a literature, in a short period of time, as has the subject of anaphylaxis. In the course of a brief decade numerous articles dealing with it have appeared, and, although in a measure polemic in nature, a substantial harvest of facts may be gathered when the chaff is cleared away.

A great deal has been published concerning hypersensitiveness to bacterial proteins, and from the data in the literature several facts seem established: Animals can be actively sensitized with dead bacteria, or with the extracts of them. The hypersensitive state is transmitted from mother to young. A refractory state is readily induced, and, in general, sensitization due to bacterial proteins obeys the same laws as does sensitization due to any other protein. Further, the symptoms resulting when a sensitized guinea pig is given an intoxicating dose of the homologous bacterial protein are in kind the same as those seen in hypersensitiveness to serum.

However, striking as is the similarity of the phenomena developing after sensitization with serum, and with proteins of bacterial origin, one apparent difference is to be noted. The injection of horse serum into a series of guinea pigs leads to the development of a state in which the animal is so sensitive that a second dose, properly administered, causes, in the majority of instances, acute lethal shock, whereas experiments published concerning hypersensitiveness to bacterial proteins give the impression that sensitization here is much less constant and much less intense. Citation of a few of the more important articles on this phase of the subject will serve to illustrate these points.

Rosenau and Anderson[1] conducted experiments on guinea pigs with extracts of cholera, typhoid, hay, anthrax, tubercle

* Read at a meeting of The Laennec, a Society for the study of Tuberculosis, The Johns Hopkins Hospital, January 27, 1913.

and subtilis bacilli. After an incubation period of 11 days or more, these animals reacted to a second dose of the specific protein, which caused no symptoms in the controls. It is noteworthy, however, that the reactions produced were never so intense as in the experiments with serum or with milk, and in no instance led to acute death.

Axamit[3] succeeded in sensitizing guinea pigs and rabbits with aqueous extracts of a variety of yeast obtained from a skin lesion. Here, again, the production of acute fatal shock was not noted.

Kraus and Steinitzer[3] produced in horses and goats "mild, or moderately severe" sensitization with typhoid bacilli.

Kraus and Doerr[4] sensitized guinea pigs with small amounts of typhoid and of dysentery bacilli, with the vibrio of cholera and with other vibrios and observed that, in only a small percentage of animals did acute lethal shock follow a second injection.

Tscharnoizkis,[5] in a large series of experiments with bacterial extracts made by heating the organisms in normal saline solution at 56° to 60° C. for an hour, concluded that the protein of typhoid, dysentery, cholera, pseudo cholera or of prodigious cultures can render animals hypersensitive; that for hypersensitiveness to develop a longer incubation period is necessary than in sensitization with serum, or with milk; and, finally, that though the state produced is a specific one, the symptoms elicited are never so intense as are those seen in hypersensitiveness to serum.

E. C. Rosenow[6] injected guinea pigs with dead pneumococci and with pneumococcus extracts. He clearly established the fact that animals can be sensitized by treatment with these substances and that the constancy with which hypersensitiveness develops depends upon the use of sufficient protein. He showed further that the hypersensitive condition is transmitted from the mother to her offspring, and that passive sensitization resulted when a normal animal was injected with the serum of an actively sensitized one.

P. Th. Müller[7] demonstrated that the constancy with which sensitization could be produced by injecting guinea pigs with *B. typhosus, coli, dysenteriæ, diphtheriæ* and with streptococci varied directly with the amount of specific protein employed.

Friedberger and Mita[8] showed that no real difference exists in the regularity with which acute death can be produced in animals sensitized with bacteria and with serum, provided the amounts of bacterial protein used for preparation and for reinjection approximate those used in producing hypersensitiveness to serum.

They interpret the failure of many observers to produce sensitization with tuberculin as due to the minimal tuberculo-protein content of that preparation, and regard the tuberculin reaction as a true anaphylactic phenomenon.

Baldwin,[9] in 1910, described in detail the manifestations produced in guinea pigs by treatment with aqueous extracts of tubercle bacilli. He demonstrated that a true sensitization could be produced with the watery extracts of this organism, the most striking results being obtained when the preliminary injection was given into the peritoneum and when the intoxicating dose was injected by the post-orbital route. He stated that as little as 0.0008 gm. of the dry protein is sufficient to sensitize a normal guinea pig; that probably even less is required, and that 0.0004 gm. suffices to produce fatal sensitization in 22 days. He also described in detail other characteristics of the state produced by the injection of tuberculo-protein and pointed out the similarity of active sensitization with it and with serum, the maternal transmission of the condition to the offspring and the possibility of causing a refractory or anti-anaphylactic state with it.

This paper is replete with valuable data and pregnant with ideas.

A. K. Krause,[10] in the following year, continued studies along the same line, investigating, among other things, the routes best suited for sensitization and for intoxication, the optimum incubation period for the development of maximum hypersensitiveness, the preparations best adapted to the work and the quantitative interrelation of these factors. He noted that practically any parenteral route by which a sufficient quantity of tuberculo-protein can be introduced may be used in sensitizing an animal; that acute anaphylaxis may be produced by toxic injections given into the post-orbital space or into a vein, and that there is no choice of method, except that of ease and availability. Krause found that sensitization can be obtained with 0.00005 gm. of tuberculo-protein, that the shortest incubation period was six days and the longest duration of the hypersensitive state was 286 days, although he believed it probable that sentitization lasts throughout life as does hypersensitiveness to serum.

Krause was unable to produce passive hypersensitiveness with the serum of sensitized animals, but stated that "further work no doubt will show that this apparent difference between the action of tuberculo-protein and serum protein is a quantitative, rather than a qualitative difference."

To all workers in the field of anaphylaxis it is a well known fact that in order to produce acute shock, amounts of protein smaller than certain established minima cannot be used. It is clear, from the published work of numerous observers, that when minimal quantities of protein, or amounts approaching this minimum are employed, the results obtained are inconstant, and that constant findings may be anticipated only when larger quantities of the material are injected.

The amounts of various sera required constantly to produce maximal hypersensitiveness have been accurately determined, but the studies of sensitization with bacterial proteins undertaken from a quantitative standpoint are few. Most of the workers in the field of bacterial anaphylaxis have designated the dosage employed by them in terms of "ösen" s, or of "cultures," apparently failing to recognize how variable the amount of organisms in a culture of different bacteria may be. Enormous amounts of bacteria, styled large sensitizing or large intoxicating doses, often signify, in reality, small amounts of protein material, inasmuch as only about 50 per cent of the dry organism, or approximately 15 per cent of the wet, is protein in nature. This fact makes it clear why many of those who have attempted to produce sensitization with

bacteria have failed, for they were working with infinitesimal quantities of essential material. Positive results can be hoped for only when better technic is employed, when quantities sufficiently large are used in the experiment.

With these facts in mind, and in an endeavor to determine if acute lethal shock can be induced constantly after sensitization with the protein of tubercle bacilli, the following experiments were undertaken.

PREPARATION OF THE TUBERCULO-PROTEIN.

Several strains of tubercle bacilli of human type were used. Two of them, H α and H β were isolated from the sputum of two patients of the Phipps Tuberculosis Dispensary of the Johns Hopkins Hospital, and one, H 39, was received from the Saranac Laboratory, through the courtesy of Dr. A. K. Krause. These strains were inoculated into many flasks of 5 per cent glycerin broth, and the growth washed with sterile distilled water until broth free. The mass of bacilli was then heated for two hours at 55° to 60° C., desiccated in vacuo and thoroughly ground to a powder. Each gram of the pulverized bacilli was then extracted with 15 ccm. of sterile distilled water, at 55° C. for from 48 to 72 hours and then filtered through a Berkefeld bougie. A clear, amber-yellow fluid was the end-product and with the addition of a little toluol as preservative, was used as the antigen. The quantitative estimations of the alcohol precipitable protein in this solution showed a content varying from 0.005 to 0.009 gm., in a cubic centimeter. In all the experiments the guinea pig was the animal of choice and, in as far as possible, animals of the same weight were used in parallel experiments.

METHOD OF INJECTION.

(a) A short series of preliminary experiments gave complete confirmation of Baldwin's observation that injection into the peritoneal cavity offers a ready route by which the protein may be introduced, leading to active sensitization of the animal, with minimal effort on the part of the experimenter, and with very little risk to the animal.

(b) For intoxication several methods were employed in the attempt specifically to shock the sensitized animals. In the protocols which follow, it will be seen that injections were made into the sub-dural space by the post-orbital route; into the right ventricle of the heart, or into the jugular vein.

For the post-orbital injections, the technic of Gay and Southard was used. A fine needle was introduced through the cocainized conjunctiva, near the median canthus of the eye, so as to skirt the eye-ball and enter the optic foramen. The warm fluid was then slowly injected into the subdural space beneath the pons. The method is easy of application, but occasionally, in spite of apparently correct technic, the solution returns through the nose.

Following the injection, even when slowly made, there is, not infrequently, transitory coma lasting 2 to 5 seconds, vertigo, sneezing and restlessness. In occasional instances, death may occur from pontile hemorrhage. Using this method, as much as 1.1 ccm. may be safely inoculated into a full grown guinea pig.

For the intracardiac injections, the technic of P. A. Lewis was followed. The chest of the animal shaved, a small needle was thrust through the fourth or fifth left interspace and when a spurt of blood returned into the syringe, the fluid was slowly injected. By this procedure, we have been able to introduce as much as 2.5 ccm. of fluid without serious consequences to the animal. Transitory restlessness, bucking move-

TABLE I.

Determination of the Primary Toxicity of Tuberculo-Protein.

Number of Guinea Pig	Weight	Mode of Injection	Amount of Protein Injected	Remarks
	Grams		*Grams*	
		Intraperitoneal		
44	310	"	0.002	No symptoms.
45	290	"	0.002	Do.
46	275	"	0.005	Do.
47	260	"	0.005	Transitory restlessness and bucking.
48	275	"	0.010	No symptoms.
49	270	"	0.020	Do.
50	300	"	0.050	Do.
192	290	"	0.100	Do.
194	320	"	0.200	Transitory restlessness and sneezing.
197	280	"	0.200	Do.
		Post-orbital		
52	250	" "	0.002	No symptoms.
56	265	" "	0.002	No symptoms. Part returned through nose.
57	275	" "	0.005	Restless, sneezing. Part returned through nose.
58	240	" "	0.005	No symptoms.
59	260	" "	0.010	Vertigo, sneezing, restless. Recovery.
62	280	" "	0.010	Transitory restlessness and sneezing.
63	230	" "	0.010	Transitory restlessness. Frequent urination.
64	220	" "	0.010	Frequent urination and defecation.
66	250	" "	0.010	Coma 20 secs. Recovery in 3 min.
67	255	" "	0.015	Part returned through nose. Sneezing, restless.
68	270	" "	0.015	No symptoms.
69	268	" "	0.015	Death immediate. Pontile hemorrhage.
		Intracardiac		
76	240	" "	0.005	No symptoms.
77	260	" "	0.005	Restless. Frequent defecation
79	250	" "	0.010	No symptoms.
82	270	" "	0.010	Death in 20 mins. Pericardial hemorrhage.
84	292	" "	0.015	Death in 50 mins. Pericardial hemorrhage.
85	280	" "	0.015	No symptoms.
86	270	" "	0.022	Dyspnea, dull. Death in 5 hrs. Hemorrhage.
87	280	" "	0.022	No symptoms.
		Intravenous		
91	300	"	0.005	Do.
92	285	"	0.010	Transitory dyspnea. Defecation.
98	310	"	0.010	No symptoms.
99	275	"	0.015	Restlessness.
100	290	"	0.022	No symptoms.
101	315	"	0.025	Do.
102	290	"	0.030	Death in 20 secs. Dilated right heart.
103	280	"	0.030	Transitory coma. Recovery in 10 mins.

ments and tachypnea are frequently noted, and many animals succumb from hemorrhage into the pericardial or pleural sacs.

For intravenous injection, the method of Friedberger was employed. A guinea pig was lightly etherized, and fastened by means of tape upon its back, the upper jaw as well as the legs being firmly fixed. The right jugular vein was dissected free and two ligatures loosely laid about it. Several hours later, after the animal had recovered its normal temperature, it was again fixed on the table and the injection made into the isolated vein. Complicated though this procedure may seem, it is readily and quickly executed and is rarely attended by any serious results to the animal. We have introduced as much as 3.5 ccm. of fluid by this method, without causing evident symptoms other than slight transitory restlessness and tachypnea.

Determination of the Primary Toxicity of the Antigen.

Injections of varying amounts of the tuberculo-protein were made by the intraperitoneal, intracardiac, intravenous and post-orbital routes, to determine the minimal lethal dose of the preparation. A study of Table I will show that the extract was practically non-toxic, for of all the 38 untreated animals injected with amounts of from 0.002 to 0.200 gm., none succumbed from the primary toxic action of the test preparation. The non-toxicity of these aqueous extracts of tubercle bacilli confirms the observation of Vaughan,[11] made in 1907.

TABLE II.

Determination of the Sensitizing Dose of Tuberculo-Protein.

Number of Guinea Pig	Weight	Preliminary Treatment	Interval	Secondary Treatment	Remarks
	Grams	*Grams Protein*	*Days*	*Grams Protein*	
		Intraperitoneal Injection		Post-Orbital Injection	
110	300	0.0005	15	0.0025	No symptoms.
111	280	0.0005	15	0.0025	Death in 1 min. Pontile hemorrhage.
112	295	0.0005	15	0.005	No symptoms.
113	290	0.0005	19	0.005	Sneezing, convulsions. Death in 30 secs. Typical post mortem findings.
114	300	0.0005	19	0.008	No symptoms.
115	300	0.0005	19	0.008	Pressure symptoms, vertigo, unrest. Recovery in 30 mins.
				Intracardiac Injection	
123	300	0.0005	14	0.005	No symptoms.
124	350	0.0005	14	0.005	Death from hemorrhage into pericardium.
125	380	0.0005	14	0.005	No symptoms.
126	400	0.0005	14	0.008	Do.
127	360	0.0005	18	0.008	Dyspnea, clonic convulsions. Death in 4 mins. Typical findings.
128	320	0.0005	18	0.010	Death from hemorrhage into pericardium.
				Intravenous Injection	
129	300	0.0005	21	0.005	No symptoms.
130	320	0.0005	21	0.005	Do.
131	300	0.0005	21	0.008	Do.
132	310	0.0005	21	0.008	Do.
133	270	0.0010	18	0.005	Do.
134	285	0.0010	18	0.005	Clonic convulsions, sneezing. Death in 18 mins. Typical findings.
135	260	0.0010	19	0.005	Clonic convulsions.
136	255	0.0015	19	0.005	Do.
137	260	0.0015	19	0.005	Death from pontile hemorrhage
138	270	0.0025	19	0.005	Sneezing, bucking, unrest. Recovery prompt.
139	285	0.0025	19	0.005	No symptoms.
140	280	0.0025	19	0.005	Vertigo, unrest, urination, defecation. Recovery prompt.
141	270	0.0035	17	0.005	Sneezing, dyspnea, pollakiuria. Recovery.
142	275	0.0035	17	0.005	Dyspnea, paresis of hind legs. Recovery.
143	260	0.0035	17	0.005	No symptoms.
144	270	0.0035	17	0.005	Do.
151	270	0.0045	17	0.005	Dyspnea, paresis of hind legs. Death in 18 mins. Typical findings.
153	290	0.0045	17	0.005	Dyspnea, bucking, clonic convulsions. Death in 7 mins. Typical findings.
154	275	0.0045	17	0.005	No symptoms.
156	255	0.0045	17	0.005	Part of fluid through nose. Restless, sneezing. Recovery.
157	283	0.0045	17	0.005	No symptoms.
158	280	0.005	17	0.005	Dyspnea, clonic convulsions. Death in 3 mins. Typical findings.
160	270	0.005	17	0.005	Clonic convulsions, gasping and bucking. Death in 5 mins. Typical findings.
161	280	0.005	17	0.005	Death from pressure?
162	290	0.005	20	0.005	Dyspnea, paresis of hind legs, hyperesthesia, fall in temp. Recovery.
163	298	0.005	20	0.005	Part of fluid lost through nose. Sneezing, unrest. Recovery.
165	270	0.008	15	0.005	No symptoms.
166	300	0.008	15	0.005	Dyspnea, clonic spasms, cyanosis. Death in 4 mins. Typical findings.
168	290	0.008	17	0.005	Coma, gasping, clonic spasms. Death in 2 mins. Typical findings.
169	260	0.008	17	0.005	Bucking, sneezing, convulsions, pareris of legs. Death. Typical findings.
170	300	0.008	17	0.005	Death from faulty technic of injection.

Determination of the Optimum Sensitizing Dose.

The attempt was made to establish the amount of tuberculo-protein which, when introduced into the peritoneal cavity of a guinea pig, would constantly sensitize it, so that a small amount of the antigen, injected by the intracardiac, intravenous or post-orbital route, would constantly elicit signs of acute hypersensitiveness. To this end, a series of normal guinea pigs were given intraperitoneal injections of tuberculo-protein varying in amount from 0.0025 to 0.025 gm., and after a period of from 10 to 24 days, these animals were reinjected with different amounts of the antigen, from 0.0025 to 0.01 gm., and the results noted. For controls, untreated

guinea pigs were given the same amount of protein by the same route as was used to shock the sensitized animals. The tables show the results of these experiments.

TABLE III.
Preliminary Treatment with Double the Sensitizing Dose.

Number of Guinea Pig	Weight	Preliminary Treatment	Interval	Secondary Treatment	Remarks
	Grams	*Grams Protein*	*Days*	*Grams Protein*	
		Intraperitoneal Injection		Post-Orbital Injection	
176	290	0.016	19	0.008	Dyspnea, clonic convulsions, coma. Death in 11 mins. Typical findings.
177	275	0.016	19	0.008	Bucking, sneezing, gasping. Death in 6 mins. Typical findings.
178	320	0.016	19	0.008	Death from pressure. Lungs collapsed and congested.
179	310	0.016	19	0.008	Clonic convulsions, coma, dyspnea. Death in 9 mins. Typical findings.
180	320	0.016	19	0.008	Transitory dyspnea, sneezing and unrest. Recovery in 4 hours.
181	320	0.016	19	0.008	Dyspnea, paresis of hind legs, coma. Death in 5 mins. Typical findings.
182	300	0.016	19	0.008	Faulty technic. Fluid returned through nose.
183	320	0.016	19	0.008	Dyspnea, clonic convulsions. Death in 8 mins. Typical findings.
				Intracardiac Injection	
185	295	0.016	19	0.008	Coma with convulsions and gasping respiration. Death in 5 mins. Typical findings.
186	280	0.016	19	0.008	Death from pericardial hemorrhage.
187	310	0.016	19	0.008	Clonic convulsions, dyspnea, coma. Death in 4 mins. Typical findings.
188	290	0.016	19	0.008	Clonic convulsions, paresis hind legs, dyspnea. Death in 12 mins. Typical findings.
189	300	0.016	19	0.008	Coma, dyspnea. Death in 50 secs. Typical findings.
190	280	0.016	19	0.008	Death from pericardial hemorrhage.
				Intravenous Injection	
171	320	0.010	19	0.008	Dyspnea, cyanosis, convulsions. Death in 6 mins. Typical findings.
172	340	0.010	19	0.008	Dyspnea, convulsions, coma. Death in 7 mins. Typical findings.
173	400	0.016	19	0.008	Gasping respiration, convulsions, paresis of hind legs. Death 11 mins. Typical findings.
174	295	0.016	19	0.008	Bucking, sneezing, convulsions. Death in 6 mins. Typical findings.
175	280	0.016	19	0.008	Clonic convulsions, gasping respiration. Death in 3 mins. Typical findings.
176	290	0.016	19	0.008	Transitory dyspnea and restlessness. Recovery.

(Four animals in this series died due to errors in technic—of the remaining 16, 14 showed lethal hypersensitiveness = 87.5%.)

Twenty guinea pigs, sensitized by the intraperitoneal injection of 0.008 gm. of tuberculo-protein, were tested 16 days later by an intravenous or an intracardiac injection of 0.005 gm. of the protein. The results are analogous to those tabulated.

Analysis of these results shows that although, in an isolated instance, it is possible to sensitize with quantities of the protein as small as 0.0005 gm., that sensitization with this dose is most irregular. It is further evident that the results are more constant and the symptoms more severe when doses larger than 0.003 gm. are used, and that in order regularly to produce maximum hypersensitiveness, an injection of at least 0.008 gm. of our preparation is necessary. It was found, too, that the optimum incubation period is between 14 and 23 days.

Using twice the amount of protein required regularly to sensitize guinea pigs, acute shock was produced by the reinjection of 0.008 gm. of protein in 87.5 per cent of the animals.

The amount of protein used for sensitization caused no variation in the incubation period required, nor did the use of repeated small doses cause any change in the end result, except that by this means more protein could be safely injected. Animals receiving protein daily, or at short intervals, and tested in less than the incubation period noted, are refractory to intoxicating injections.

The quantity of tuberculo-protein required regularly to elicit the signs of anaphylaxis in a properly prepared animal varies from 0.0025 to 0.008 gm., with 0.005 gm. as an efficient intoxicating dose in well prepared animals.

In six guinea pigs sensitization persisted for 490 days, and we agree with Krause that in all probability further work will show that this state of hypersensitiveness persists throughout the life of the animal.

Maternal Transmission of the Hypersensitive State to the Offspring and the Duration of this Inherited Hypersensitiveness.

Six female guinea pigs, actively sensitized 18 days before by the intraperitoneal injection of 0.008 gm. of tuberculo-protein, were caged with two normal untreated bucks. Four of these females became pregnant and each gave birth to three young. Paralleling the work of Rosenau and Anderson on the maternal transmission of hypersensitiveness to horse serum, we sought to exclude milk as the transmitting factor. Six of these young guinea pigs were therefore placed to nurse an untreated female and the offspring of this normal mother placed to nurse the hypersensitive female. After four, six and nine weeks, respectively, the young of the sensitized and of the non-sensitized females were tested, with the following results:

Two guinea pigs born of sensitized mother No. 188, and nursed by her, succumbed with acute shock; one failed to react. Three of the six young, born of sensitized females Nos. 189 and 196, and nursed by untreated guinea pigs, died in acute shock, whereas three showed only slight symptoms and recovered. None of the five guinea pigs born of normal mothers showed any symptoms when injected with tuberculo-protein.

This short series of exchange experiments shows that hypersensitiveness to tuberculo-protein is transmitted from the mother, and that the milk plays no rôle in this transmission.

Twelve guinea pigs born of five untreated females, impregnated by sensitized males, were not hypersensitive to tuberculo-protein. Females sensitized before the beginning of pregnancy, early, or late in the course of it, in the few instances studied, transmitted the hypersensitive state to the offspring. The regularity with which hypersensitiveness is transmitted to the young varies, to some extent, with the degree of hypersensitiveness of the mother.

Two animals with inherited hypersensitiveness, tested 120 and 175 days after birth, respectively, showed signs of acute hypersensitiveness.

Passive Sensitization to Tuberculo-Protein.

Twenty-two attempts were made to transfer hypersensitiveness to tuberculo-protein from actively sensitized guinea pigs to untreated animals of the same species. Quantities of fresh serum or of citrated whole blood obtained from 16 hypersensitive animals, varying from 1 to 6.5 ccm. in amount, were injected into the peritoneal cavity of normal guinea pigs. Of the 22 animals so treated, three died before they were tested. The remaining 19 were given post-orbital injections of 0.008 gm. of the tuberculo-protein, 22 to 42 hours after the preparing dose. Four of these animals succumbed in 3 to 18 minutes, with the symptoms of acute hypersensitiveness, and post mortem showed the typical massive pulmonary emphysema, sub-epicardial hemorrhages and delayed coagulation time; three died as the result of faulty technic; and in the remaining 12, no symptoms developed. The controls were all negative.

In this series of experiments, it was striking that passive sensitization was inconstant in its development, but that it could be brought about with greater regularity when the donor of the serum or blood had been treated with at least 0.008 gm. of the protein.

Passive heterologous hypersensitiveness from rabbits to guinea pigs was successfully produced in three of 14 attempts. In each instance the rabbit received, intraperitoneally, 0.005 gm. of protein per 100 gm. of body weight, and 18 days later 4 ccm. of the rabbit serum, in divided doses, were injected into the peritoneal cavities of untreated guinea pigs. The guinea pigs were then tested after an incubation period of 40 hours by an injection of 0.008 gm. of tuberculo-protein injected into the post-orbital space.

To recapitulate:

These experiments confirm the already demonstrated facts that:

1. A protein substance can be obtained by the extraction of tubercle bacilli with water, and with it animals can be actively sensitized.

2. A refractory condition to this protein can be produced.

3. The hypersensitive condition is transmitted from mother to young.

These experiments establish further that:

1. Active sensitization induced by treatment with this protein may be as regular in its development and as intense in its manifestations as is that produced by treatment with other proteins.

2. Passive homologous and heterologous hypersensitiveness can occasionally be produced with the blood or with the serum of an actively sensitized animal.

3. The material transmission of the hypersensitiveness does not take place through the milk.

4. The regularity with which maximum hypersensitiveness can be produced is largely dependent on the use of a sufficient amount of protein in preparing and in testing the animals.

To warrant the application of the demonstrated facts to assist in interpreting the phenomena that develop when tuberculin is administered to a host infected with the tubercle bacillus, the identification of the protein used in these experiments with the essential protein of tuberculin seemed desirable.

Some evidence that such an identity could be established had already been furnished by Baldwin and by Krause, who produced lethal anaphylactic shock by injecting tuberculous guinea pigs with old tuberculin.

In the following experiments it will be shown that tuberculous guinea pigs do develop symptoms of hypersensitiveness following the injection of "tuberculo-protein," of "old tuberculin," or of albumose-free tuberculin into the heart or into the subdural space; and further, that cross sensitization with these preparations is readily produced.

The Intoxication of Tuberculous Guinea Pigs.

The guinea pigs used in these experiments had each received an injection of 0.001 gm. of a culture of H 39 beneath the skin of the right groin 61 days before the tests were made. To bring about the intoxication of these animals, post-orbital or intracardiac injections of the several proteins were made.

Of 12 tuberculous animals tested, one of the four injected with old tuberculin showed signs of hypersensitiveness, two of the four tested with albumose-free tuberculin succumbed with signs of acute shock, and one of the four tested with "tuberculo-protein" developed lethal hypersensitiveness.

Cross Sensitization Experiments.

Preparation of the proteins tested.

The proteins used in these experiments were as follows:

A. Tuberculo-protein, the protein obtained by the aqueous extraction of ground tubercle bacilli in the manner already detailed.

B. "O. T. Protein," the protein obtained from old tuberculin. The tuberculin itself was used in only a few experiments, inasmuch as the large content of glycerin and of salts make it an undesirable antigen. To remove these constituents, the tuberculin was treated as follows: 4 ccm. of old tuberculin, diluted with distilled water to about 12 ccm., were treated with an equal amount of 10 per cent sodium hydrate for 36

hours at 55° C., then filtered and precipitated with ten volumes of absolute alcohol. The white flocculi formed were dried in vacuo, redissolved in distilled water, neutralized with $\frac{n}{1}$ hydrochloric acid and again precipitated with absolute alcohol. The precipitate, after desiccation in vacuo, was then ground and the white powder thus obtained used as antigen. Although undoubtedly rich in peptone, this material is less irritating to the guinea pig and is appreciably less toxic than commercial old tuberculin.

C. "A. F. Protein"—Albumose-Free Tuberculin. Inasmuch as this tuberculin contains no nitrogenous material except that from the tubercle bacillus and asparagin, it has a very low primary toxicity. In the experiments to follow, the untreated commercial preparation was therefore employed.

METHOD OF IDENTIFYING THE PROTEINS.

No attempt was made chemically to identify the preparations used. The facts obtained were derived from experiments made to determine if sensitization of an animal with one protein caused hypersensitiveness to the others. The method was as follows:

A number of guinea pigs were each given eight daily intraperitoneal injections of 60 mgm. of the powdered "O. T. Protein," and after an incubation period of 17 days were tested by an intracardiac injection of 0.015 mgm. of "tuberculo-protein," or of 2 ccm. of "A. F. Protein." Similarly, guinea pigs sensitized by two intraperitoneal injections each of 1 ccm. of A. F. Tuberculin after 17 days were given a post-orbital or an intracardiac injection of 0.015 mgm. of "tuberculo-protein," or 1 ccm. of "A. F. Protein"; and guinea pigs sensitized by an intraperitoneal injection of 0.015 mgm. of "tuberculo-protein" were similarly tested with "A. F. Protein."

In none of the experiments was the "O. T. Protein" used to intoxicate sensitized animals because of its primary toxicity, due probably to its peptone content.

These experiments clearly demonstrated that preliminary treatment of guinea pigs with "O. T. Protein," "A. F. Protein," or with "Tuberculo-Protein," causes the development of hypersensitiveness to "A. F. Protein" and to "Tuberculo-Protein."

This is sufficient evidence to prove the general assumption concerning the identity of the essential protein of tuberculin used to demonstrate the reaction in man, with the tuberculo-protein shown to produce classical hypersensitiveness in animals. The demonstration of this fact justifies the application of the data obtained in the experiments on animals with tuberculo-protein to the interpretation of the phenomenon known as the tuberculin reaction.

Wolff-Eisner,[12] v. Pirquet,[13] Baldwin,[1, c.] Krause,[1, c.] Hamman and Wolman,[14] and many others regard this phenomenon as a manifestation of hypersensitiveness to tuberculin. For this view the presumptive evidence is strong. The facts which support this hypothesis may be briefly summarized as follows:

All the manifestations of typical hypersensitiveness to protein can be produced in guinea pigs by treatment with aqueous extracts of tubercle bacilli. Guinea pigs can be sensitized with albumose-free tuberculin and with old tuberculin that has been freed of glycerin and made poor in salts. And sensitization with any of these products causes the animal to react to injections of the others.

Hypersensitiveness to tuberculin develops within 7 to 15 days after infection with the *B. tuberculosis*.

Tuberculous animals can occasionally be intoxicated with tuberculo-protein, developing symptoms of hypersensitiveness.

The passive transference of hypersensitiveness from a tuberculous man to normal guinea pigs has been successfully accomplished[15] and positive results have likewise been obtained when the serum of a sensitized animal has been injected into an untreated one.

The type of the reaction symptoms and the development of them in an infected host after the administration of minimum doses of tuberculin are likewise suggestive facts.

This evidence justifies the interpretation of the tuberculin reaction as a manifestation of true hypersensitiveness.

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THE ANCIENT OFFICE OF CORONER.*

By David I. Macht, M. D.,

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If there be found a slain person in the land which the Lord thy God giveth thee to possess it, lying in the field, and it be not known who hath slain him; then shall thy elders and thy judges go forth, and they shall measure unto the cities which are round about the one that is slain. And it shall be that the city which is nearest unto the slain person, even the elders of that city shall take a heifer, which hath not been wrought with, which hath not drawn in a yoke; and the elders of that city shall bring down the heifer unto a rough valley, which is neither tilled nor sown, and they shall break the neck of the heifer in the valley; And the priests, the sons of Levi, shall come near; for them the Lord thy God hath chosen to minister unto Him, and to bless the name of the Lord; and after their decision shall be done at every controversy and every injury; And all the elders of that city who are nearest unto the slain person shall wash their hands over the heifer, the neck of which is broken in the valley. And they shall commence and say, Our hands have not shed this blood, and our eyes have not seen it. Grant pardon unto Thy people Israel, whom Thou hast redeemed, O Lord, and lay not innocent blood in the midst of Thy people Israel; and the blood shall be forgiven unto them. And thou shalt put away the guilt of the innocent blood from the midst of thee, when thou wilt do what is right in the eyes of the Lord. Deut. XXI, 1-9.

This passage from the Bible will illustrate the fact that a legal inquiry into all cases of violent death or deaths due to unknown causes has been practiced by enlightened nations from time immemorial. So, indeed, we find that in all civilized countries of our day, there is some form of preliminary investigation or other, wherever there is reason to believe that a deceased person came to his death through violent or unfair means, or by culpable or negligent conduct of himself or others, and not through pure accident or mischance. The necessity for such an investigation is self-evident and is recognized by all, and it is usual to conduct it without delay and by competent officers, and, if necessary, without anybody being accused: in fact it is to afford evidence of the necessity or otherwise of anybody being accused that the investigation is of greatest use. The mode of conducting such an investigation, however, varies in different countries. In France it is conducted by an officer somewhat similar to our district attorney and called the *procureur de la république*, who is assisted by a proper medical expert; in Germany, there is a similar judicial officer named the *Staatsanwalt;* in Russia, Denmark, and other European countries the procedure is essentially the same as in France or Germany, that is the case is investigated by the ordinary state's attorneys, who call for assistance upon expert medical men. It is to the English law that the honor belongs of designating an especial officer for this important function, the coroner, who represents the king as a caretaker of the lives of the people, and provides that every violent death or sudden death with cause unknown shall be subject to public inquest by a jury of not less than twelve good and lawful citizens. This is still the practice among most of the English-speaking nations, that is in England and her Colonies, with the exception of Scotland, and in most of the United States.

The coroner is so-called *à coronâ*, because he is an officer of the crown, and this name, or variations of it, have been used for many years. He was called *coronarius*[1] in the reign of Henry II. He was styled *custos placitorum coronæ*[2] in the reign of Richard I, and in the Magna Charta and subsequent statutes he is known as *coronator*.

The office of coroner is of so great antiquity that its commencement is not definitely known.[3] Its origin is usually ascribed to the Articles of the Eyre of 1194, but it is probably much earlier. By some it is said to be coeval with that other distinctly English office, that of the sheriff, and to have been ordained with the latter office to keep the peace when the earls gave up the wardship of the county. At any rate we know that coroners existed in the time of King Alfred,[4] and this office is also mentioned in the charter granted by King Athelstan to the monastery of St. John of Beverley in 925.[5] We thus see that this office is nearly a thousand years old.

The duties of the coroner in his earlier days embraced a much wider sphere of activity than at the present time.[6] Thus from 4 Edward I. St. 2 (*Officium Coronatoris*) it appears that:

a coroner of our lord the king ought to inquire of these things: First, when coroners are commanded by the king's bailiffs or by the honest men of the county, they shall go to the places where any be slain, or suddenly dead or wounded, or where houses are broken, or where treasure is said to be found, and shall forthwith command four of the next towns, or five, or six, to appear before him in such a place; and when they are come thither, the coroner upon the oath of them shall inquire in this manner, that is, to ask, if it concerns a man slain, if they know when the person was slain, whether it were in any house, field, bed, tavern, or company, and if any, and who were there, etc. It shall also be inquired if the dead person were known, or be a stranger, and where he lay the night before. And if any person is said to be guilty of the murder, the coroner shall go to their house and inquire, etc.

Thus we note that his duties were not confined to cases of sudden or violent death. Indeed on examining the old documents we find that they extended over a wide range of criminal matters and even to civil pleas (Gross[7]). In the thirteenth century coroners were the principal agents in bringing all sorts of criminals to justice. They held inquests not only in cases of sudden, violent, or unnatural deaths, but also in cases of serious bodily injury, burglary, arson, rape, prison-breaking, and concealment of treasure-trove or wreck. They received the declarations of approvers, and heard criminal accusations of one person against another, the final trial being reserved for the eyre. They kept, moreover, a record of outlawries, and received the confession and abjuration oath of felons who had fled to sanctuary. They furthermore some-

* Paper read at a meeting of The Johns Hopkins Medical Society, January 6, 1913.

times exercised judicial powers, by virtue of their appointment, and tried criminal pleas; and also conducted jury trials in ordinary civil pleas, either taking the place of the sheriff, or more commonly associated with him. In default of the sheriff, or if he was a party in a suit, royal writs were regularly executed by coroners; and furthermore, occasionally they were employed by the crown to transact purely ministerial or administrative business, assisting or superseding the sheriff. Indeed throughout the thirteenth century the coroner acted as a check on the former. The coroner was representative not merely of the king but also of the people, being elected in the county court, from the county, and "with the assent of the whole county"; and being a man of substance and credit, and a knight, one of the original qualifications required being the knighthood,[8] was less liable to be oppressive and obnoxious to the people than the sheriff, who often bought his appointment from the crown, frequently lived in some other county, and generally regarded his office as an instrument of private gain. A survival of this historical relationship between the two offices is still exemplified, by the well known legal maxim that the coroner is the only officer empowered to arrest the sheriff.[9]

In England the coroner is appointed for life, or *quamdiu se bene gesserit*, for time of good behavior. In the United States, as we shall see later, the appointment is for a specified period of time, generally for two or four years. Coroners are exempt from serving offices which are inconsistent with their duties. They are also privileged from being summoned on juries, and from arrest while engaged in the execution of their duties.[10]

In England the coroner may appoint a deputy coroner to act during his illness or absence.

According to British law, a coroner can be removed from office only by decree of the High Court of Justice after conviction of extortion or misdemeanor, or by writ of the Lord Chancellor after proof of misbehavior or inability in office.[11] Similarly in the United States, in those states where he is appointed by the governor, he is responsible for his action directly only to the governor.

Coroners in England may logically be classified into four classes:[12]

First: Official Coroners. These are the Lord Chief of Justice and all the judges of high courts; who are coroners by virtue of their office, but never act as such.

Second: Franchise Coroners. These hold their appointment by virtue of ancient charters granted to special households or communities. Thus there is the coroner of the verge or the king's household; again, the wardens of the Stanneries of Cornwall may act as coroners; and, lastly, the Lord Mayor of London is a coroner, but does not act as such.

Third: Borough Coroners. These are appointed by the borough councils.

Fourth: The most important of all, the county coroners. The county coroners were elected from time immemorial by the vote of all the free-holders of the county. These elections, however, gave rise to so much scandal and abuse, that Parliament in 1888 by a clause in the Local Government Act decreed that in the future all county coroners should be elected by the county councils. This was a salutary reform, for the county councils generally exercise wise discretion and choose worthy candidates with both legal and medical qualifications. The county coroners as appointed and qualified by the Coroners Acts of 1887 and 1892 are essentially the coroners of to-day.

By the Coroners Act of 1887, the functions of the coroner are defined as follows:

> **Where a coroner is informed that the dead body of a person is found within his jurisdiction, and there is a reasonable cause to suspect that such person has died either a violent or an unnatural death, or has died a sudden death of which the cause is unknown, or that such person has died in prison, or in such place or under such circumstances as to require an inquest in pursuance of any act, the coroner, whether the cause of death arose within his jurisdiction or not, shall, as soon as practicable, issue his warrant for summoning not less than twelve nor more than twenty-three good and lawful men to appear before him at a specified time and place, there to inquire as jurors touching the death of such person as aforesaid. (Sec. 3 (1).)**

Under this Act he is empowered to summon medical witnesses and order a post mortem (S. 21). If any person is found guilty of homicide the coroner shall commit him to prison for trial. He may accept in his discretion bail in case of manslaughter. Since the abolishment of public executions he must hold inquests on bodies of executed criminals. The duty to inquire into cases of treasure-trove is still present in the Act of 1887. In the United States this duty has been abolished, except in so far as it is the coroner's duty to take charge of the valuables found on unknown dead persons and to deposit them for safe-keeping in a proper public institution.[13] In the city of London by the City of London Fire Inquest Act of 1888, the coroner still holds inquests in cases of loss or injury by fire.

The Act of 1892 deals chiefly with the appointment and duties of deputy coroners in England. We cannot here go into a more detailed examination of the Coroners Acts of 1887 and 1892, but all those especially interested should read the excellently annotated edition of those Acts by Jervis.[14]

The most important function of the coroner, the function by virtue of which he possesses considerable magisterial powers, and through which he differs from all analogous officers on the European continent, is the holding of jury inquests.

"Inquest" or *inquisitio* is an interesting survival of a word which is associated with the birth of a new system of procedure, and which in mediæval England was a common generic term applicable to all forms of investigation, whether used for judicial or administrative purposes. There is good reason to believe, as pointed out by Gross,[l. c.] that the coroner's inquest and coroner's jury, had an important bearing on the development of the modern trial jury. The coroner's jury in the thirteenth century consisted of representatives of the four neighboring *villatæ*, or townships, that is, the one in which the body was found and three others. Now the activity of these four townships was not confined merely to coroner's

inquests. Other duties and responsibilities in connection with criminal administration were often imposed upon them collectively. It has, therefore, been surmised that the coroner's jury or jury of inquiry, gradually developed into the traverse or trial jury of the later days.

The coroner's jury is selected from all the "good and lawful" men of the county. Only a few classes are exempt, such as peers, clergymen, members of Parliament, barristers, and some others. In the United States, there are similar exceptions—state officers, lawyers, physicians, and a few others being excused.

In order to serve on the jury of inquest the jurors must each and every one of them view the remains of the deceased and must be sworn in by the coroner to perform diligently their important duty (S. 4. (3)).

The law requiring the jury to hold the inquest *super visum corporis* that is only after viewing the dead body, has been often criticised and objected to.[14] The objections, however, are mostly of a sentimental nature.[15] I do not think there is any valid objection to this procedure. Indeed, it helps the jurors to gain a clearer idea of the case, and adds to the dignity and solemnity of the occasion.

Having been sworn in, the coroner appoints the time and place for holding the inquest proper and the jury adjourns.

Perhaps a clearer idea of the working of a coroner's jury and inquest may be gained by describing briefly the procedure followed by the coroners in this city.

Having decided to hold an inquest a coroner communicates with the captain or lieutenant of the nearest police station, by means of a telephone, or more conveniently and quickly through a police signal box, to which he has a key. The police captain then sends two or more officers to his aid. Together with the officers he goes to some busy public thoroughfare in the vicinity of where the dead body is lying, and they accost any passer-by whom the coroner deems suitable. He touches the person lightly on the shoulder and says:

In the name of the State of Maryland I summon you to meet on a coroner's jury.

This obligates the party to serve. In case of evasion or escape he is liable to imprisonment at the coroner's order. In a similar manner other jurors are selected or "picked," to use a colloquial expression, until a sufficient number have been assembled. Although twelve men are all that are necessary, it is customary to impanel two or three more, so as to have a full number, in case one or more of the jurors be prevented from attending the inquest through some unforeseen circumstance. The coroner and jury next go in a body to the place where the slain or dead person is lying, and the jurymen view the remains. The coroner then, *super visum corporis* or in the presence of the dead body, swears the jurors in, the oath being as follows:

In the presence of the Almighty God you do solemnly promise and declare that you will dilligently inquire and true presentment make as to the cause how, where, when and in what manner ——— ——— came to his death and such other facts as might be related to the case on behalf of the State of Maryland.

The coroner then fixes the time and place of inquest and adjourns the jury. In designating the time for holding the inquest he usually tries to make it convenient both to himself and to the jurors, who in this city are not paid for their services, and that is generally in the evening. The place for holding the inquest is usually at the police station of the district, where appropriate quarters are provided for the purpose. Inquests may lawfully be held on Sunday.[16]

FORM OF INQUEST REPORT.

STATE OF MARYLAND, BALTIMORE CITY, TO WIT:

AN INQUISITION, taken at.....
in the City and State aforesaid, on the.....day of.....
in the year of our Lord nineteen hundred and.....before me,.....one of the Coroners of the State for the City aforesaid, upon the body of.....
then and there lying dead, upon the oaths of

.....	.....
.....	.....
.....	.....
.....	.....
.....	.....

good and lawful men of the State and City aforesaid; who, upon being duly sworn, and charged to enquire when, where, how, and after what manner the said.....
.....
came to h death, do say upon their oaths that h.....
.....
.....
.....
.....
.....

IN WITNESS WHEREOF, as well the aforesaid Coroner, as the Jurors aforesaid, have to this Inquisition put their hands and seals, on the day and year aforesaid, and at the place aforesaid.

.....*Coroner.* [SEAL]

..... [SEAL]	..... [SEAL]
..... [SEAL]	..... [SEAL]
..... [SEAL]	..... [SEAL]
..... [SEAL]	..... [SEAL]
..... [SEAL]	..... [SEAL]
..... [SEAL]	..... [SEAL]

Preparatory to the inquest the coroner with the help of the police, summons witnesses and gathers in all the evidence he can, and if necessary orders an autopsy. The coroner has the same powers as a judge to compel witnesses to testify.[17] The witnesses before giving their testimony must be sworn in.[18] They are liable to punishment for disobedience.[19] The coroner has a right to order an autopsy even against the consent of the relatives of the deceased.[20] He has the right even to exhume a body,[21] and where a case is a proper one for an inquest it is a misdemeanor maliciously or intentionally to burn or otherwise dispose of the body.[22]

At the appointed time and place, the jury meets, and the coroner opens the coroner's court and conducts the inquest. He summons the witnesses, swears them in, and gathers the evidence. The jury may ask the witnesses questions. Here, also, the pathologist or physician who has performed the post

mortem, delivers his report. In all important cases the coroner furthermore has a member of the state's attorney's office at his side to advise him, and all evidence is taken down by a court stenographer.

Having heard the evidence the coroner summarizes the case and asks the jury to deliberate and return a verdict. Instances have occurred where coroners have unduly influenced the jury in their deliberations.[23] It is therefore customary for the coroner and all other persons to go out and leave the jurors alone. When the jury has agreed on the verdict, the foreman whom the coroner had previously designated, announces the decision. The verdict is then written down and signed by the coroner and each of the jurors on a special printed form as shown on opposite page. After that the coroner discharges the jury.

One inquest may be held on the bodies of several persons if they were killed by the same cause and died at the same time.[24]

The coroner being a judge, enjoys certain special privileges the same as other judges. Thus he is not liable for error or mistake.[25] He cannot be held for defamatory words used at an inquest.[26] He can turn anyone out of the room where the inquest is held.[27] He has the power of arresting and detaining the accused after the inquest (S. 5 (1)).

It is customary for the coroners in this city, for the good of the public, to make reports of the various cases they investigate to the police department, and they are required by law to make monthly reports to the police commissioners of all the cases coming under their jurisdiction. (Balto. City Charter (1898), S. 297).

It will be seen that the holding of a jury inquest is quite a complicated procedure, which takes considerable time and imposes a good deal of inconvenience on the jurors, and an additional expense on the State. The question, therefore, arises, when shall an inquest be held and when not? The decision on this point is left entirely to the discretion of the coroner, although the law broadly lays down the indications. According to the Public General Laws of Maryland:

No coroner shall summon or hold any jury of inquest over the body of any deceased person where it is known that the deceased came to his death by accident, mischance or in any other manner, except where the said person died in jail, or where there are such circumstances attending the death or case as to amount to a strong probability or reasonable belief that the deceased came to his death by felony.[28]

Unless, therefore, the coroner's preliminary investigation reveals facts concerning the death sufficient to create in his mind a reasonable belief that it resulted from some unlawful means, or unless the deceased died in jail, he is not justified to hold an inquest and impose an extra burden upon the jurors and the State.

Coroners have been criticised for holding too many unnecessary and expensive inquests,[29] and in the case of a coroner in Lancaster County, Pennsylvania, who sued to recover fees for an inquest in a case of death from paralytic stroke, the supreme court refused the payment, the opinion handed down reading as follows:

Where there is no ground for suspecting that death was not a natural one, it is a perversion of the whole spirit of the law to compel the county to pay for such services.[30]

The coronership is often regarded by the public at large and by a great many medical men as a sort of a sinecure. The coroner is supposed to draw his salary and have nothing more to do than hold an occasional inquest, say once or twice a month. This idea is due to the general ignorance on the part of the public concerning a coroner's duties. Although the conducting of jury inquests is the most important of his functions, that is but a small part of his work. It is the coroner's duty to investigate, or to use a technical term to "make inquiries" into, a large number of cases of death. The following classes of deaths must be all referred to the coroner and investigated by him, and the bodies cannot be buried without his certificate.

I. **All violent deaths.** This includes homicides, suicides and accidents.

II. **All sudden deaths,** whether violent or otherwise. By sudden deaths we generally understand deaths occurring after an illness of less than twenty-four hours.

III. **All suspicious or unnatural deaths** from whatever cause, such as poisonings, drownings, burnings, still-births of unmarried women, deaths of infants of unmarried women occurring within a few days after their birth, etc.

IV. **All deaths where there has been no attending physician.** Parenthetically, I may mention, that under this heading fall also the Christian Scientists.

V. **Deaths in prison.**

In all the above cases the coroner has a right to and should insist, that they be brought to his notice, and not leave it to the discretional judgment of the physician who may have been in attendance (if there has been one) as to whether he shall be notified or not. In cases of accidents or other violent deaths, the coroner should investigate all cases, even where the accident did not suddenly terminate life, but where the victim lived several days, and died afterwards from some complication brought on by the injury.[31] This opinion has been sustained by courts.[32] Perhaps some idea of the work done by coroners in this city may be gained if I will merely state that in the Northwestern District, the coroner has on the average at least about thirty and sometimes more cases of death to investigate or hold an inquest over in one month. In the Central and Northeastern Districts there are just as many and often more.

We have seen at the beginning of this paper that the coroner's office is well nigh a thousand years old. It is therefore not surprising that it has received its share of both praise[33,34] and adverse criticism.[35,36] The commonest objection raised is that of the inherent incongruity of an office requiring a knowledge of law and medicine.[37] Such criticism is a platitude and quite unjustifiable, for medico-legal matters, from the very nature of their subject, demand a harmonious combination of legal and medical knowledge or experience;

whether they be dealt with by a single officer such as a coroner, or by two officials, such as the medical examiner and a lawyer in some states, is all the same. To abolish the office merely in order to divide the work between two specialists is in the words of Wyatt Johnston "an extreme measure and not actually called for."[38] As a matter of fact it would seem that a preliminary investigation by a properly trained medical man, such as a coroner should be, empowered to summon and examine witnesses under oath and followed if necessary by a subsequent inquest by an intelligent jury, is the best form of procedure. That this officer should preferably be a medical man stands to reason, for obviously the most important questions to answer are "how" and "in what manner," a person has come to his death; the questions "when" and "where" are not so intricate as to need great legal acumen.

We may draw, I think, an interesting analogy between the coroner and that other officer, whose calling is even older than that of the coroner, whose function is to watch over and preserve the life and health of the people, and the importance of whose position is beginning, even at this very time, even in this era of specialization, to be more and more appreciated—the family physician. It is the latter and not the specialist that knows best each and every member of the families entrusted to his care—their weaknesses, their private life, their relations to the outer world; and it is he who in emergency, in moments of anxiety and sorrow, can best take in the situation, can diagnose, advise, and bring relief. He, too, can best decide, if anything unusual has happened, and he is the one that can judge best, if expert help or specialists are needed. So, with the coroner. Being a man well-known in the community, a competent physician, versed in the rudiments of law, acquainted with the world at large—he can and will dispose most quickly and efficiently of all the ordinary cases; at the same time, if anything unusual or important should happen, he always can and will obtain all the expert aid he wants. Thus in this city the coroners always have at their disposal the hearty cooperation and assistance of an expert pathologist and a chemist on the one hand, and all the legal advice they desire from the state's attorney's office on the other.

But, just as the ordinary family physician is now-a-days expected to be acquainted to some extent at least with all the branches of modern medicine, and keep in touch with the latest progress and advances of his science, so ought the coroner to have at least a reasonable amount of medico-legal training. Speaking of the training of medical officers in forensic medicine, Prof. Dr. P. Dittrich, of Prag, says: we cannot be expected to know all, but

Ein gewisses minimum ist man zu verlangen verpflichtet[39]

and conscientiously speaking that minimum ought to be a "good deal."

What are some of the subjects that should come and do come under the head of coroner's duties? Perhaps I can review them best by discussing briefly six cases which happened to come under my jurisdiction within 48 hours last summer.

Case I.—Was that of a dead infant—a "still-born" the mother called it. To investigate such a case carefully, a number of very important problems present themselves. In the first place it is necessary to determine if possible the age of the fœtus; then it is well to know how long it has been dead. The question as to the cause of death is a very important one. It brings up the consideration of abortions and infanticide. Furthermore, if the birth was a natural one, was the child alive when it was born and died after delivery, or was it dead in utero? The latter point may be of great consequence in civil processes, in regard to legitimacy and inheritance.

Case II.—A poor man living alone with strangers was taken sick and after a brief illness died, without having been attended by a physician. This case shows the importance of a post mortem examination in all obscure cases. Not knowing anything about the deceased, and not getting any history as to his past or to his illness, the question as to the cause of death is practically impossible to answer without the pathological examination. The problem of determination of personal identity is one of the most interesting, one of the most important, and one of the most difficult chapters of legal medicine.

Case III.—A white woman went to church one Sunday night, and on her way suddenly felt "bad." She was taken to the nearest doctor's office, and there died in a few minutes. This is an illustration of the cases of "sudden deaths" mentioned above, which must be referred to the coroner. The cause of death in this case could be positively determined from the past history of the deceased. On inquiring into it, it was learned that she had been suffering from organic heart disease. The case illustrates the importance of a careful inquiry into the past history of a dead person, especially in cases like the present, where there is great objection to and no urgent necessity of making an autopsy. The coroner must often be able to make a correct diagnosis of the cause of death from the history of a case.

Case IV.—A child was brought to one of the city hospitals suffering from the effects of drinking a can of lye. Lye poisoning is quite common among the children of poor negroes, and this is but an illustration of an unnatural death through poisoning. The case, however, brings up the very intricate and extensive subject of toxicology, a science by itself, but with some of the various points of which every medico-legal officer ought to be familiar.

Case V.—A young man was found dead lying on the bed in his room with all doors and windows locked, and the gas jets turned on, evidently a case of suicide. Suicides, however, are often very difficult to differentiate from homicides; a very careful investigation of the environment and all the attending circumstances must therefore be made. Furthermore, this case brings us again into the field of toxicology—poisoning by illuminating gas. Again it is desirable to find out how long the body had been dead, which requires a knowledge, by no means easy to acquire, of the signs and phenomena of death, and of post mortem changes. Then again, if the suicide is a stranger, extreme ingenuity may be required to establish his identity. Furthermore, the motive for the taking of life touches upon the subject of sanity and insanity, all of which come within the province of legal medicine.

Case VI.—A boy was brought to a hospital in an unconscious state. The mother stated that he was playing on a high express wagon, that he was pushed off by some party, and falling hurt his head. A doctor was summoned, who diagnosed the case as a concussion of the brain, and sent the patient to the hospital. The child died on the following day with the symptoms of meningitis; a lumbar puncture seemed to confirm the diagnosis. The X-ray specialist thought that there was a very fine linear fracture on one side of the skull. The autopsy, ordered by the coroner revealed a definite linear fracture of the skull, but on the opposite side of the head from that indicated by the X-ray man. There was general congestion of the brain, but no sign of meningitis. This case

illustrates, how difficult it is sometimes to determine the cause of death especially when two sets of symptoms are present. Some of the physicians were of the opinion that death was due to meningitis; others attributed it to a fracture of the skull. If a meningitis had existed at the time of the accident, it would have been of the greatest importance in a civil suit, for in one case death might have been due to an accident, in the other to natural causes. This case touches also upon the subject of wounds, their nature and classification, the evidence presented by them as to their causation, and their relation to death. I will not go into the consideration of criminal negligence and responsibility which this case raises.

These are but a few of the subjects with which a coroner ought to be familiar. Are all coroners acquainted with them? We must confess, too often they are not. That is why the office has come into disrepute, and that is why the nestor of our profession, Abraham Jacobi, in one of his addresses speaking of coroners in New York exclaims with his characteristic force: "

What is their preparation for that office? They are elected by the people at the tail end of the ticket, while their office should be one coming next to that of mayor and far above that of sheriff, with which the coronership is often classed.

Why and when are they nominated at all?—usually about or after midnight, when the nominating committee is bored and sleepy. Are the nominees good doctors, first-rate lawyers . . . . ? Usually the men, with some praiseworthy exceptions, are but little known in their district, they furnish a surprise to the reading public, who wonder and submit.

And what are some of the subjects that should come and did come under the head of coronership? Let me mention a few: The exact knowledge of the signs of life, the changes caused by death, by no means an every day's easy task; the cause of death in the still-born or the premature child; the proofs and disproofs of infanticide; the explanation of sudden death in the very young. The discovery of poisons is one of the most difficult tasks of the chemist. The responsibility of physical defectives belongs to the coroner's domain—a murder may have been committed in the first attack of epilepsy; simulation must be diagnosticated from actual disease, and the results of infectious diseases of the most common type often lead to crime. All this must be well understood to distinguish the sick person from the criminal, all this and much more belongs to the office of the coroner.

The trouble with the coronership in America is the trouble with so many other departments of our government. The laws are good; their administration and execution are often bad. We need not new laws, but a loftier conception and more conscientious execution of the old ones!

But already we note the signs of an awakening, and a brighter outlook for the future is before us.

As I conclude this paper, I cannot but recall a famous maxim from the Talmud:

לא מקומו של אדם מכבדו
אלא הוא מכבד את מקומו

"It is not the office that giveth honor to the man; it is the man that bringeth honor to the office." "

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DR. EPHRAIM McDOWELL, "FATHER OF OVARIOTOMY": HIS LIFE AND HIS WORK.*

By AUGUST SCHACHNER, M. D., Louisville, Ky.

During a visit to Germany in the summer of 1911, I talked with several Germans about Dr. Ephraim McDowell, and grew convinced that neither the man nor his work were as thoroughly understood as they deserve to be. This discovery became my *chief* reason for investigating Dr. McDowell's life, and for my endeavor to prepare a clear presentation of him and his work.

In the present paper lack of time compels me to present the

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subject in a direct and concise form, foregoing in many instances details of circumstances and reasons for reaching and holding certain conclusions.

According to the family tradition, the ancestors of Dr. Ephraim McDowell emigrated from Scotland to North Ireland, during the Protectorate of Cromwell, about the middle of the seventeenth century.

Ephraim McDowell, the great-grandfather of Dr. Ephraim McDowell, fought in the English Revolution. At the age of 16 he was one of the Scotch-Irish Presbyterian defenders of Londonderry, during the troubles in 1688, and aided in resisting the besieging forces of James II in the memorable siege of 1689. His wife was Margaret Irvine, his first cousin. With his two sons, John and James, and his daughters Mary and Margaret, he emigrated to America, landing in Pennsylvania. It is believed that his wife died in Ireland. The date of his arrival in Pennsylvania, where he remained several years, is unknown, possibly, as thought by some, September 4, 1729. In Pennsylvania his son John, who was the grandfather of Dr. Ephraim McDowell, married the thrice-wedded Magdalena Wood, and it was here that Samuel, the father of Dr. Ephraim McDowell, was born, on October 29, 1735. In 1737 Ephraim McDowell, his son John, his son-in-law, John Greenlee, with his wife Mary McDowell Greenlee, moved by way of the lower Shenandoah Valley to what is now Rockbridge County, Virginia, near the present town of Lexington. They were the first three settlers in that region.

The great-grandfather of Dr. Ephraim McDowell died at the age of about 100. He lies buried in Rockbridge County, Virginia.

Capt. John McDowell, the father of Samuel McDowell, and the grandfather of Dr. Ephraim McDowell, fell in a battle with the Indians on Christmas day, 1743. He left three children, Samuel, James and Sarah. Samuel, the oldest, born in Pennsylvania, October 29, 1735, was the father of Dr. Ephraim McDowell. Two years later John McDowell moved with his family to Virginia. Samuel, as he grew up, received a good education for those times, one of his instructors being his relative, the distinguished Dr. Archibald Alexander. On the 17th day of January, 1754, in Rockbridge County, at the age of 18, he was married to Miss Mary McClung, daughter of John McClung and Elizabeth Alexander. Miss McClung, of Scotch parentage, was born in Ireland on October 28, 1735. Samuel McDowell and his wife Mary had 11 children born to them. When twenty years old he fought in the French and Indian War. He served under General Washington, and was present at the battle of Braddock's defeat. In 1774 he served as captain in Dunmore's War, and in the battle of Point Pleasant was an aide-de-camp to General Isaac Shelby, who afterwards became the first governor of Kentucky, and whose daughter later became the wife of Dr. Ephraim McDowell. Samuel was a colonel in the war of the Revolution, and with his regiment served under General Green at the battle of Guilford's Court House, and throughout Green's campaign against Cornwallis.

Preceding the Revolution, Samuel McDowell and Thomas Lewis represented Augusta County in the Convention of 1775 at Richmond, and protested against government by any ministry or parliament in which the people were not represented. They were delegated to address to George Washington, Patrick Henry, Benjamin Harrison, and other delegates from Virginia in the Continental Congress, a letter of thanks and approval of their course. In 1776 Samuel McDowell was a member of the Convention held at Williamsburg, Virginia, which instructed the delegates to the Continental Congress to declare the colonies free and independent.

He was appointed in 1782 by the Virginia legislature one of the commissioners to settle land claims in what was then a portion of Virginia, but afterwards became the state of Kentucky.

In 1783 he came as a surveyor with his family over the Wilderness Road, and took up his residence in Fayette County. In that year, at Harrodsburg, he, with two others, presided over the first court held in Kentucky. The next year he moved to Mercer County, in which Danville was situated. According to Collins, he was made president of all the early Kentucky conventions, nine in number, including the one that framed the Constitution of Kentucky. During his presidency in 1792, Kentucky was admitted to the Union.

In religion he was a member of the Presbyterian Church. He remained upon the bench until a few years before his death, and was known as Judge McDowell, to distinguish him from one of his sons, Samuel. After a long and useful life, during which he enjoyed the fullest measure of confidence and esteem throughout his state, he passed away, September 25, 1817, at the age of 82, at the residence of his son, Colonel Joseph McDowell, near Danville, Kentucky.

Dr. Ephraim McDowell was born November 11, 1771, in that portion of Augusta County, Virginia, that is now called Rockbridge County. He is generally referred to as of Scotch-Irish stock. Correctly speaking, he was born in the colony of Virginia, under the British flag, of Scotch parentage. Both sides of his house were Scotch. They emigrated to America by the way of, and after some residence in, Ireland. The Scotch-Irish reference in this, as in most other instances where it is employed, is misleading, and is based upon the residence in Ireland and not upon any mixture of Scotch and Irish blood. He was the ninth of eleven children, and the sixth son. When about 13 years of age, he moved from the place of his birth to the place of his future activity, Danville, Kentucky.

He received the best education that those early times and frontier conditions afforded, which, however, according to our present standard, might rightly be termed limited. Worley and James, who conducted a school at Georgetown, and later at Bardstown, were among his teachers. He also attended the Academy at Lexington, Virginia. His subsequent reputation as an athlete, while at the University of Edinburgh where he was successfully pitted by his class against an Irish professional in a foot race, lends color to the view that at school he was fonder of outdoor sports than indoor studies.

Later he studied medicine for two or three years with Dr.

Alexander Humphreys, of Staunton, Virginia, who was a graduate of the University of Edinburgh.

In 1793 and 1794, McDowell attended the University of Edinburgh. It is believed that while there he gave especial attention to anatomy and surgery. Apparently dissatisfied with the surgical lectures, or at least feeling a desire for more instruction in this line of work, he became a member of the private class of John Bell, who, in addition to being an able surgeon, was a clear and forceful teacher, and a man of charming personality. It is generally thought that from Bell's influence, together with his lucid lectures upon the diseases of the ovary and his statement that some day surgery would relieve those suffering from ovarian troubles, the seed sprung from which developed the operation of ovariotomy.

Indications justify the belief that he left Edinburgh without his degree, although some of his relatives claim that he secured it. He returned from there in 1795 and began the practice of medicine at his home in Danville where he remained until his death.

In 1817 the Medical Society of Philadelphia, the most distinguished of that time in this country, publicly recognized McDowell's ability, and in 1825 he received an honorary degree from the University of Maryland. This appears to be the first degree that was ever conferred upon him. Lunsford P. Yandell, Sr., suggests that this came through John P. Davidge, one of the founders of the University of Maryland, for Davidge was a friend and contemporary of McDowell at the University of Edinburgh.

Situated as he was, in a frontier city, favorably known and extensively connected, and with what was at that time unusual, a training in one of the best, if not the very best of the foreign universities, it is needless to say that an extensive practice covering what was then the entire southwest rapidly sprang up.

Hardly any anecdotes of his childhood or personal recollections of his manhood are known. He is described as erect and tall, nearly 6 feet, and inclined to corpulency, with a florid complexion and lustrous black eyes. He was a ready wit and fine conversationalist. In an unpretentious way, he was fond of music; he would sing English and Scotch songs with comic effect, accompanying himself with his violin upon which he performed with ordinary ability. He mingled freely with all classes of his townspeople, displaying the modesty and simplicity of a great man. He is said not to have used tobacco in any form, and to have been temperate in his habits. He was neat in person and invariably dressed in black, wearing a silk stock and ruffled linen.

He inclined to surgery; the medical side of his work he transferred as much as possible to his partner, and in his instructions to his pupils, he urged them not to rely too much upon drugs. His foreign training and Scotch origin explain his preference for Cullen and Sydenham in medicine, and Burns and Scott in literature. He was no writer; his only contributions to medical literature are said to be two reports in the Eclectic Repertory and Analytical Review upon his ovarian operations.

At the age of 31, he married Miss Sarah Hart Shelby, who was then in her eighteenth year. She was the daughter of Governor Isaac Shelby, Kentucky's first governor. Six children were born to them, two sons and four daughters. Three of the children survived him. Through the influence of his wife, he became a member of the Episcopal Church. Several years before his death, he retired to his country home called Cambuskenneth, located about two miles from Danville, but did not give up the practice of medicine.

His death occurred while still in the full vigor of life. The illness began suddenly, while he sat in his garden eating strawberries. The chief symptom was great pain, followed by nausea and later by fever, which is said to have lasted fourteen days, when he died (possibly of an acute appendicitis). In his death, which, according to some, occurred on the evening of June 20, and according to others, June 25, 1830, in his 59th year, he preceded his wife ten years. They were both buried in the family burying ground, near Danville, at Travellers Rest, the home of his father-in-law. In 1872, Dr. John D. Jackson, of Danville, seconded by Dr. Lewis A. Sayre, started a movement which was completed through the Kentucky State Medical Society in 1879, and had, as its results, the removal of the remains of Dr. Ephraim McDowell and his wife, to Danville and the erection of a shaft over their graves.

On December 13, 1809, fourteen years after he began the practice of medicine, he was called to see a Mrs. Crawford, who lived in Green County, some 60 miles from Danville. She was thought to be pregnant and had exceeded her time. McDowell, after an examination, explained to her the nature of her condition and his proposed plan of relief.

Exactly what passed between McDowell and his memorable patient is mere speculation and will never be known. The operation at the time of its performance, received, considering its importance, comparatively little attention even from McDowell himself. An account of it was not published until about seven years later and then only after considerable urging on the part of his friends.

This much we know, that Mrs. Crawford yielded to McDowell's judgment and made the journey to Danville on horseback, it is said resting the tumor upon the horn of the saddle.

There is a tradition that McDowell's life was threatened by an angry mob for his rashness in performing the operation. This will never be satisfactorily proven or disproven. It seems, on reflection, reasonable to assume that this story has with time become exaggerated. McDowell was generally underrated by many and specially maligned by his enemies. He was held, however, by the greater part of his people to be easily the foremost man in medicine, and also considered a leading citizen in his community. Mrs. Crawford's evident entire willingness to undergo the operation is emphasized especially by the distance and difficulties under which she made the journey. No doubt the proposed operation was known to every one beforehand and in all likelihood, as is customary in small places, even to-day, where news is at a premium and where the tedium of the lives of the people is broken by their interest in their neighbors' affairs, there were comments of all kinds. In fact it is said that his nephew, Dr. James McDowell, whom he brought

up and who was his partner, made several attempts to dissuade him from operating and agreed only at the last moment to be present, and assist for fear of the damage he would sustain in his practice in the event of failure of the operation.* There does not appear, however, enough ground upon which to base the story of an organized effort to do him bodily harm in the event of failure.

After the lapse of seven years following the first ovariotomy and at the repeated urgings of another nephew, William, and others, he was prevailed upon to prepare a report of the first three cases. This was forwarded in 1816 to his old teacher, John Bell, to whom it is believed he was indebted for the idea, but fell into the hands of John Lizars, owing to Bell's absence in Italy in quest of health.

Another copy was sent in the autumn of 1816 to Philip Syng Physic of Philadelphia, with a request that it be published if found worthy and this, like the first, received no attention.

His nephew, William, who was the bearer of the report to Physic then turned to Dr. Thomas C. James, who has passed into history as the modest, amiable and benevolent professor of midwifery in the University of Pennsylvania, and one of the editors of the Eclectic Repertory.

Professor James, who placed confidence in McDowell and his nephew, took the time to study and then communicate the report to his pupils, amid their applause, and later publish it in the Eclectic Repertory and Analytical Review (Vol. VII, 1817). The original report, which, we feel, in view of its importance and interest should be reproduced in full as far at least as it deals with the first case, is as follows:

In December, 1809, I was called to see a Mrs. Crawford, who had for several months thought herself pregnant. She was affected with pains similar to labor pains, from which she could find no relief. So strong was the presumption of her being in the last stage of pregnancy that two physicians, who were consulted on her case, requested my aid in delivering her. The abdomen was considerably enlarged and had the appearance of pregnancy, though the inclination of the tumor was to one side, admitting of an easy removal to the other. Upon examination, *per vaginam*, I found nothing in the uterus, which induced the conclusion that it must be an enlarged ovarium. Having never seen so large a substance extracted, nor heard of an attempt or success attending any operation such as this required, I gave to the unhappy woman information of her dangerous situation. She appeared willing to undergo an experiment, which I promised to perform if she would come to Danville (the town where I live), a distance of sixty miles from her place of residence. This appeared almost impracticable by any, even the most favorable conveyance, though she performed the journey in a few days on horseback. With the assistance of my nephew and colleague, James McDowell, M. D., I commenced the operation, which was concluded as follows: Having placed her on a table of the ordinary height, on her back, and removed all her dressing which might in any way impede the operation, I made an incision about three inches from the musculus rectus abdominis, on the left side, continuing the same nine inches in length, parallel with the fibers of the above-named muscle, extending into the cavity of the abdomen, the parietes of which were a good deal contused, which we ascribed to the resting of the tumor on the horn of the saddle during her journey. The tumor then appeared full in view, but was so large that we could not take it away entire. We put a strong ligature around the Fallopian tube near the uterus, and then cut open the tumor, which was the ovarium and fimbrious part of the Fallopian tube very much enlarged. We took out fifteen pounds of a dirty, gelatinous-looking substance, after which we cut through the Fallopian tube and extracted the sack, which weighed seven and one-half pounds. As soon as the external opening was made the intestines rushed out upon the table, and so completely was the abdomen filled by the tumor that they could not be replaced during the operation, which was terminated in about twenty-five minutes. We then turned her upon her left side, so as to permit the blood to escape, after which we closed the external opening with the interrupted suture, leaving out, at the lower end of the incision, the ligature which surrounded the Fallopian tube. Between every two stitches we put a strip of adhesive plaster, which, by keeping the parts in contact, hastened the healing of the incision. We then applied the usual dressings, put her to bed, and prescribed a strict observance of the antiphlogistic regimen. In five days I visited her, and much to my astonishment found her engaged in making up her bed. I gave her particular caution for the future, and in twenty-five days she returned home as she came, in good health, which she continues to enjoy.

This report was met with indifference and incredulity on the one hand and ridicule on the other.

The original paper sent to Bell, which fell into the hands of Lizars, was published seven years after McDowell's report in connection with one of Lizars' failures, and it was this that awakened Europe and, through reaction, aroused America more than McDowell's own publication.

The second operation in 1813, four years after the first, was upon a negress. In this the ovary was exposed and incised, allowing a gelatinous substance and blood to the amount of about one liter to escape, but the ovary was not removed owing to the firmness of its adhesion to the *vesica urinaria* and *fundus uteri*. She recovered from the operation, had no more pain and was able to pursue her occupation. The third operation, and the last to be included in his first report, was performed May, 1816, or three years after the second. Like the second, it was upon a negress and in this case he removed a *scirrhous ovarium* weighing six pounds.

His second communication, also published in the Eclectic Repertory, embraced descriptions of his fourth and fifth patients, who, like the others, except the first, were negresses. The fourth was operated upon April, 1817. It was a *scirrhous ovarium* weighing five pounds. Although she made a recovery from the operation and it was the smallest of all, it gave him the most trouble at the time and was not as satisfactory in the end results as the others.

The fifth, who was operated upon May 11, 1819, had been tapped four times before the operation. Many adhesions were encountered. Sixteen liters of gelatinous fluid were discharged from the tumor and abdomen. She died of peritonitis on the third day. The tumor was a dermoid cyst.

These were the only cases that McDowell reported; the exact number of these operations he performed will never be known. Samuel D. Gross collected three additional cases, all white, making eight in all, four in white and four in negro women. Five operations were complete and three were incomplete. Of

* In McDowell's own account of the operation he says, that his nephew, James McDowell, did assist him.

the five complete operations, there were two in white and three in negro women, with one death among the latter, the mortality of the completed operations thus being 20 per cent. William, his nephew and also at one time a partner, is the authority for the statement that his uncle performed the operation in all 13 times.

McDowell's surgery was not confined to that of the ovary. He performed lithotomy 32 times without a death. One of his lithotomy cases, James K. Polk, later became president of the United States. He operated for hernia and performed all the operations known in his time.

After a careful search the writer has been unable to find sufficient evidence to justify the belief that McDowell ever performed Cæsarean section or that he ever returned to Europe after leaving the University of Edinburgh. By preference he operated on Sunday mornings.

Considering the importance to humanity of McDowell's work, he has been overlooked to an unpardonable degree, but what must we say when we come to that brave woman, Jane Todd Crawford, who successfully balanced her heroism against McDowell's genius and thereby joined with McDowell in emancipating countless millions of human beings of all nations and creeds in time to come, from a terrible condition from which a miserable death alone supplied the avenue of escape.

Peaslee in 1870 estimated that McDowell had added 30,000 years to the active life of womanhood in the 30 years prior to 1870 in the United States and Great Britain alone through the operation of ovariotomy. This in itself, would be quite enough to entitle Ephraim McDowell and Jane Todd Crawford to the lasting gratitude of humanity.

McDowell's operations, by demonstrating to the world the feasibility and safety of entering the abdominal cavity, became the cornerstone of abdominal surgery. To estimate even approximately at present the thousands of human beings that are annually saved and the countless hundreds of thousands of years that are annually added to human life through abdominal operations, would be a task well nigh superhuman. Abdominal surgery has reached such proportions that ovariotomy is but one of its smaller divisions, and when we think that even this bids fair to be extended and still further improved, we begin to realize the priceless gift and the enduring obligation that humanity owes to Ephraim McDowell and Jane Todd Crawford.

For more than a century the heroine of this story has passed from one writer to the next as Mrs. Crawford, of Green County. No one seems to have thought it necessary to establish her identity that she might take her proper place in history.

After an investigation fraught with many difficulties, extending over many months, involving an enormous correspondence and assuming at times a discouraging outlook, I feel justified from the records in my possession, in presenting the following history of her:

Jane Todd Crawford, who richly deserves to share with McDowell the honor and glory of an international memorial for her heroism, was born in Rockbridge County, Virginia. She was the sister of Samuel Todd, of Frankfort, Kentucky. Thomas Crawford and his wife, Jane Todd Crawford, with Thomas Mitchell, who in 1768 in Virginia had married Rachael, the sister of Thomas Crawford, moved to the waters of Caney Fork, nine miles southeast of Greensburg, arriving there November 5, 1805.

It must be remembered that Kentucky was still largely a wilderness and, owing to Indians and other dangers, emigrants moved about during the early periods not singly, but in groups. This was four years before Mrs. Crawford was operated upon. There is a record to show that Thomas Crawford and his wife, Jane, transferred to John Motley, 427 acres of land for $1900, "cash in hand," December 8, 1810, one year after the operation. The land was afterwards known as Motley's Glen.

Five children were born to them, Hon. Thomas Howell, Crawford, who was mayor of the city of Louisville in 1859 and 1860, Rev. James Crawford, a Presbyterian minister, Samuel Crawford, Alice Craig Crawford, who married William Paul Brown, and a daughter who died in infancy. Dr. Samuel D. Gross has proven conclusively that Mrs. Crawford did not give birth to a child after the ovariotomy.

As the daguerrotype camera was not introduced into the United States until 1839, it is not reasonable to suppose that any photograph was ever taken of her and in all likelihood no portrait of her was ever painted. All efforts to procure what would seem a trustworthy description of Mrs. Crawford, and more details germane to the operation, have so far failed.

There is a tradition in the Mitchell family that McDowell made no charge for the operation, but that Mr. Crawford presented him with an honorarium so large that, considered in the light of that period and the contracting parties, it is out of reason to suppose the story credible, and is mentioned simply as one of the many errors and traditions that confronted us in our search.

The story of Jane Todd Crawford's subsequent movements, her death and the discovery of her grave which had been forgotten for about a century, is akin to a romance, but entirely too long for the present paper. Stripped of its details, a long search and an extensive correspondence brought the writer in touch with Mr. J. K. Mitchell, a lawyer of Osborne, Kansas, and a grandnephew by marriage of the heroine. Mitchell's vigorous efforts resulted in enlisting the aid of the Rev. J. H. McArthur, a Presbyterian minister of Sullivan, Indiana, who discovered the grave in the Johnson Cemetery ten miles northwest of Sullivan.

Since the family bible, in which the family records were kept, was burned during the fire that destroyed the house of Rev. James Crawford, it is practically impossible to determine her exact age. The date of her death has been given variously as 1841, 1842 and 1843. The inscription on her tombstone reads:

JANE CRAWFORD
Died
Mar. 30, 1842
Aged 78 years
Blessed are the dead who die in the Lord.

According to this she survived the operation 33 years.

In the spring of 1912 the writer started a movement to preserve and memorialize the house in which McDowell lived and performed the ovariotomy.

The importance of rescuing this historic landmark situated in what is now the questionable quarter of Danville, and used as a negro boarding house, is too plain to require more than mere mention.

With this end in view, the writer addressed the Kentucky State Federation of Women's Clubs at their annual meeting at Mammoth Cave, May 29, 1912, and urged them in view of being the first beneficiaries of McDowell's work, to unite in saving this structure. He said in part:

If benefits to the human race are to be the standard by which we measure the usefulness and importance of a life, I am prepared to defend the statement that the importance of Dr. Ephraim McDowell's life overshadows that of either Washington or Lincoln, and that the house in Danville in which the ovariotomy was performed, should be more sacred not only to an American, but to the entire human race, than any other structure upon the whole American continent.

It has been fashionable for centuries to ignore the real benefactors of the human race, and to rush madly forward with monuments and memorials to statesmen and especially military leaders. This is a remnant of feudalism that is still in us. It is a legacy from the time when might was right even in smaller matters, as it still is to a degree in international matters, when we, more fondly than we do to-day, worshipped power and pomp at the expense of equity and reason. I do not wish to be understood as detracting from the statesman and the warrior, but I do wish to point out the benefits of the work of such a man as Ephraim McDowell as compared with the very greatest statesmen and military leaders. The moulding of a nation, the advancement of a particular people by a wise statesman, and the leadership of a successful army in a just cause, are matters that do not admit of any division of opinion. Since, however, many statesmen are forcible but not wise, and many military leaders brave and daring in an unjust cause, it is obvious that both harm and good are equally dispensed by these two popular idols. And even when the statesman is wise, and the military leader is fighting a just cause, they affect but one people and that they affect perhaps for one period, quite enough to justify their activities I will admit, as we all must.

Compare, however, this with Ephraim McDowell, whose life has affected all people. When he, for the first time on December 13, 1809, performed, before the time of anæsthetics, and without trained assistants and the usual conveniences that to-day are considered as almost indispensable, the operation of ovariotomy, he conferred upon womanhood in particular, and mankind in general, a benefit as great as any that has ever been conferred upon the human race in this or any other country and in this or any other age.

I am sure that no one will for a moment, dispute the magnitude of this gift to humanity, but I am not sure as to how many of us can really measure the greatness of this deed.

Since women were the first beneficiaries of his work, it seems entirely natural for the women of Kentucky to rescue the house in which this memorable deed was performed and which has added to the honor and glory of Kentucky more than all her other achievements combined, great as they are.

When this is accomplished, there should be an international movement to erect a joint monument befitting the services to the memory of Dr. Ephraim McDowell of Danville, and Jane Todd Crawford.

I am here to make an appeal to you to unite in rescuing from oblivion, what should be the most cherished and sacred structure in the entire Republic.

Even though the house should by some misfortune be destroyed, the spot should be memorialized. One feels like saying that it will be akin to savagery to ignore the spot where this deed immeasurable for its good, was consummated.

The appeal was favorably acted upon by the Kentucky State Federation of Women's Clubs. With commendable promptness a memorial committee was created. The writer made a number of efforts, some before and many during the half year following this action by the Federation, to persuade the owner of the building to place a valuation upon the same.

Although a man in affluent circumstances, he has resisted all entreaties towards placing a price upon the structure. As to whether John Gill Weisiger, the present owner, will ever be willing to sell this structure, that this shrine that spells more than volumes can describe, can be memorialized, that is a question that time alone can answer.

NOTE.—Since reading this paper before the Johns Hopkins Hospital Historical Club, a letter has been received from Mr. John Gill Weisiger offering to sell the house for $10,000, the offer to remain in effect for five days. The price has been considered as being considerably higher than expected, but we hope that the Kentucky Federation of Women's Clubs who have created a McDowell Memorial Committee wil be able to secure this house, and keep it as a memorial to Dr. Ephraim McDowell and Mrs. Crawford.

FIG. 1.—The McDowell Coat of Arms.

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FIG. 2.—Dr. Ephraim McDowell. From a portrait in possession of his granddaughter, Mrs. William M. Irvine, Richmond, Ky.

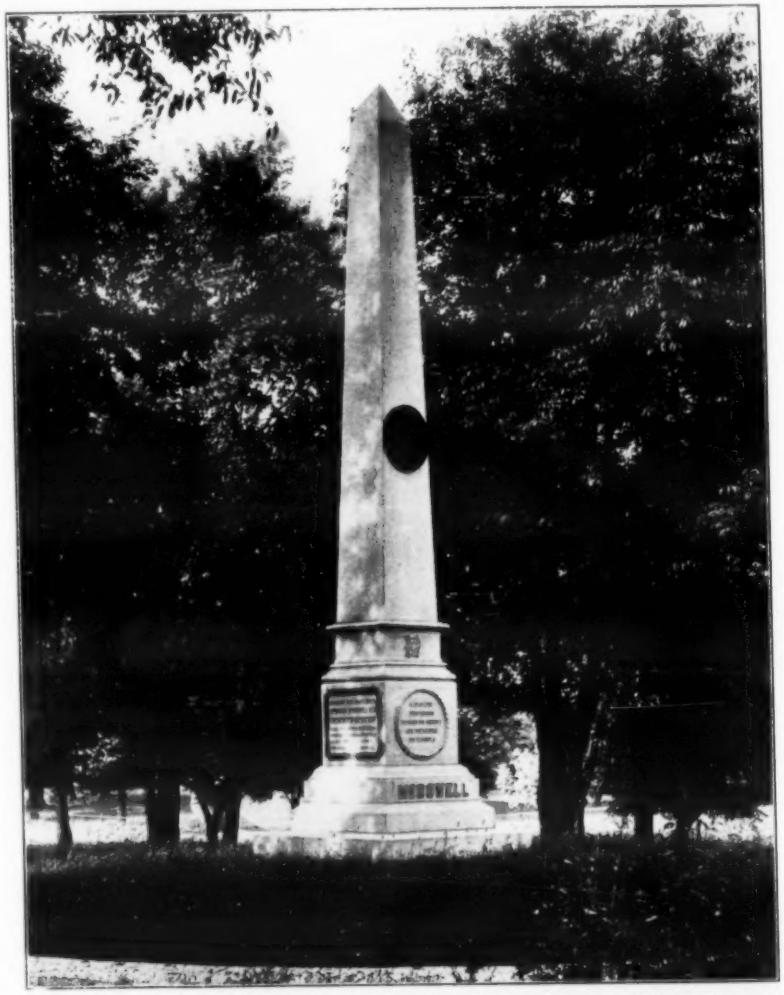

FIG. 7.—Dr. McDowell's present burial place in Danville, to which his remains were removed in 1879 through the efforts of the Kentucky State Medical Association.

FIG. 3.—The house in which Dr. McDowell lived and performed the first ovariotomy, showing the present character of the street.

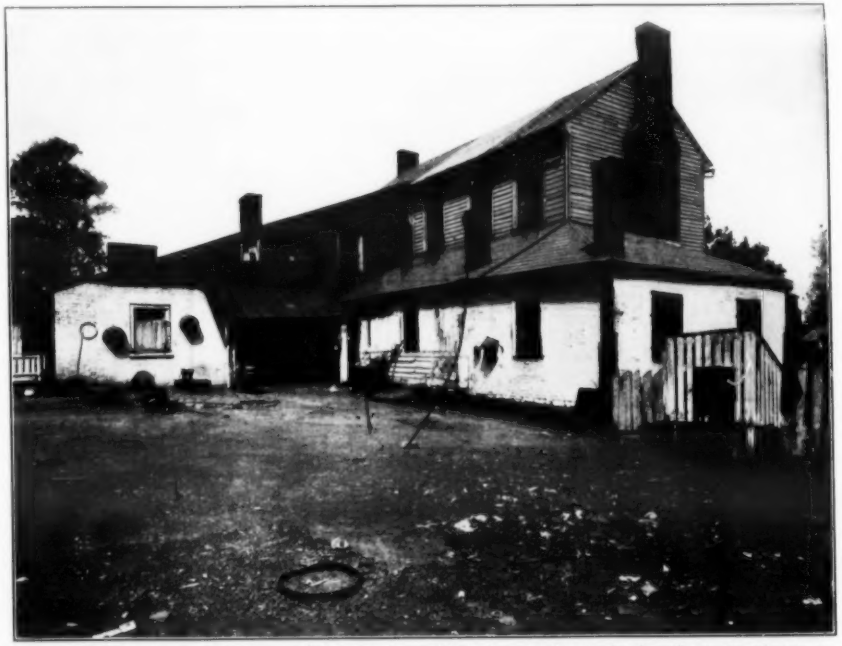

FIG. 4.—Premises and rear of house in which he performed the first ovariotomy, showing the slovenly condition.

FIG. 5.—Dr. McDowell's first burial place in the family burying ground at Travellers Rest, the homestead of his father-in-law, Gov. Isaac Shelby. The grave, as indicated by the arrow, was just beyond the slab seen in the center of the picture.

FIG. 6.—The remaining fragments of the slab that covered Dr. McDowell's first grave. By permission of Isaac Tevis, Esq., Shelby City, Ky. (The inscription was brought out by brushing it with whiting.)

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NOTES ON NEW BOOKS.

Surgery and Diseases of the Mouth and Jaws. By VILRAY PAPIN BLAIR, M. D. Illustrated. $5. (*St. Louis: C. V. Mosby Company, 1912.*)

Within a very brief period several works on this specialty have appeared, so that any surgeon desiring to make a thorough study of these conditions will have no difficulty in learning what are the best measures to employ. Blair's work is a good one for the specialist to have on his shelves; it covers the ground in a satisfactory manner. He shows how much can be done to improve a deformity, such as a receding chin, but it is to be hoped that further studies will enable the surgeon to perform less disfiguring operations in certain cases than is now possible. The progress along these lines has been great, but there is need of still more work in this branch of surgery, before the results will be as good as they ought to be or compare with those obtained in other surgical fields. This book will serve as a valuable stepping stone in that direction.

Text-Book of Anatomy and Physiology for Nurses. By ELIZABETH R. BUNDY, M. D. Second Edition Revised and Enlarged. Illustrated. $1.25. (*Philadelphia: P. Blakiston's Son & Co., 1913.*)

The author says that the scope of the second edition of her text-book of Anatomy and Physiology for Nurses has been extended to include more definitely the subject of physiology. Her endeavor has been so to associate the consideration of the structure and functions of the various parts of the body that a comprehension of their anatomy and physiology may be simultaneously attained. Dr. Bundy has written the anatomical portions of her work very completely and in a manner calculated to be easily comprehended by the classes her volume is intended to reach. It is clear and not too much overburdened with detail. There is, however, an almost complete neglect of the histological structure of the body tissues.

That portion of the book—fully one-third the volume—given to the consideration of bone and muscle is very complete and well illustrated. The so-called "clinical and obstetrical notes" are always of interest and of practical significance.

The notes on physiology in this section though good are extremely brief.

The whole subject of the alimentary tract together with the consideration of foods and their digestion is rather too much condensed. This is also true of the respiratory system and the kidneys. The circulatory and nervous systems are very thoroughly and well discussed—especially from the anatomical standpoint.

The section on regional anatomy is admirable and very practical. In conclusion one might say that as an anatomy the book is excellent but as a physiology it falls far short of the ideal.

Practical Cystoscopy. By PAUL M. PILCHER, M. D. Illustrated. $5.50. (*Philadelphia and London: W. B. Saunders Company, 1911.*)

Pilcher's Cystoscopy does not fill a long-felt want, but can be safely recommended to students. The author divides his work into seven parts: 1. The technic of cystoscopy; 2. The diseased

bladder; 3. Diseases of the prostate; 4. Diseases of the ureter; 5. The functional activity of the kidneys; 6. Diseases of the kidneys; and 7. Therapeutic uses of the cystoscope. It covers much ground as can be judged from these headings, but the ground is only lightly worked over.

This book is bigger in form than it should have been—the print is unnecessarily large and the margins far too wide. Had it been cut down to a reasonable shape and size it would have been more welcome and could have been produced more cheaply. There are a number of needless illustrations, and some of them are of poor quality, but others are excellent.

A Text-Book of Pathology for Students of Medicine. By J. George Adami, M. D., etc., and John McCrae, M. D., etc. Illustrated. $5. (*Philadelphia and New York: Lea & Febiger, 1912.*)

The authors of this excellent volume state that it is to be regarded not as an abbreviation of their larger book, but as a new work with a somewhat different purpose. The general style of treatment is similar to that of the "Principles of Pathology," and represents an effort, aimed confessedly at the medical student, to present the facts and phenomena of pathology. These facts and phenomena are compared to bricks, and it is suggested that we must concern ourselves, not only with the raw materials, but with the plan and uses of the completed structure to be built from them.

The division is made into general and special pathology. The section on general pathology covers approximately 330 pages of the 708, and includes chapters on inflammation, the progressive and regressive tissue changes, and tumors, which are authoritative in character.

In the part devoted to special pathology, the treatment of the cardio-vascular system may perhaps be singled out for its especial excellence.

Amongst the introductory material may be found some innovations; for there are discussions of histology, physiology, immunity, the Mendelian law, etc. Teratology is fully covered, and Dr. Adami's ingenious classification of tumors is the one used.

The publishers' work has been well done, the type and illustrations being clear and satisfactory.

There can be little doubt that this is the best text-book in English at the present time, and it is to be recommended to the student of pathology.

A Reference Handbook of the Medical Sciences, Embracing the Entire Range of Scientific and Practical Medicine and Allied Science. By various writers. Third Edition, Completely Revised and Rewritten. Edited by Thomas Lathrop Stedman, A. M., M. D. Complete in eight volumes. Volume I. Illustrated by numerous chromolithographs and 611 fine half-tone and wood engravings. Nine hundred and thirty-six pages. (*New York: Wm. Wood & Co.*)

Since the first appearance of this valuable handbook in 1885 the advance in medicine and allied sciences has been so great and so rapid that there is much in the first volume of the new edition which was not dreamed of more than twenty-five years ago. In all sciences there has been immense progress during these years, but perhaps in none have there been such revolutionizing discoveries as in medicine, and this makes a new edition of this work at this time especially acceptable to the profession. The second edition appeared more than ten years ago, and is now in measure out of date. The number of pages in the new volume are 928, eighty more than in the first edition, and whereas the original volume ran from "Aac to Cat," the new one includes only words from "Aac to Bac." This shows in part how many new articles there are, and also indicates that many of the articles are much longer now than they were. There is some difference in the arrangement of the articles, for instance, in the first volume appeared "Anus and rectum: Diseases of." To-day the title reads "Anus: Diseases of the. See Rectum and anus: Diseases of the." There will doubtless be many such changes, and when the entire edition is published it will make but little difference to the reader, and is only noted to show that encyclopedia makers have various methods for cross-references, methods which naturally will not approve themselves to all readers.

Some of the articles are accompanied by longer or shorter bibliographies. There seems to be no method in this and the references are not, throughout, printed alike; that is in one article titles will be abbreviated, in others, given in full; and the method of noting the volume and page does not always agree. Except as regards appearance this is a point of small importance, but we believe there should be some system as to the introduction or omission of bibliographies. A severer reflection is that some of the references are very old, and indicate either that the article has not been revised or that the author has been careless in not adding more modern ones.

This applies also to the use of illustrations, about which there seems to be no general rule. Many of these might have been improved especially the colored ones, which do not appear to us satisfactory, in view of the excellent color reproduction which is now possible. In some instances old illustrations have been entirely omitted, and new ones take their place.

The first volume promises well and we doubt not that the handbook is going to be a most valuable addition to our medical libraries and that it will be heartily welcomed by the profession. The difficulties of the undertaking are very great, and no encyclopedia can be perfect or please everyone, but we are sure that under the editorship of Dr. Stedman this work will be an honor to him, and thus to the publishers as well.

The Illness and Death of Napoleon Bonaparte. By Arnold Chaplin, M. D. 70 cents. (*London: Hirschfeld Brothers, Ltd., 1913.*)

This book should be of universal interest,—to students and admirers of Napoleon, as it is an accurate description of the illness which closed a remarkable career,—to the medical profession as it clears up certain important points in regard to diagnosis and treatment,—and to the laity, because it is written in such a way as to be easily understood. In dealing with his subject, the author discusses in detail the history of the illness for the three years prior to death, the results of the post-mortem examination, criticisms of the diagnosis and treatment, and in conclusion sums up the entire case. In an appendix is given a biography of each of the physicians in attendance upon the distinguished patient while in St. Helena, a short account of the specimens in the museum of the Royal College of Surgeons of London, and of the exhumation of Napoleon in 1840. The book is a fair and just criticism of the faulty diagnosis and treatment, written from an impartial standpoint.

Modern Methods in Nursing. By Georgiana J. Sanders, Formerly Superintendent of Nurses at the Massachusetts General Hospital, Boston. Illustrated. $2.50 (*Philadelphia and London: W. B. Saunders Company, 1912.*)

This is a very comprehensive work of over 800 pages, and one which is sure to prove acceptable to many nurses, since it covers the ground so thoroughly. It is divided into 24 chapters. Miss Sanders takes up first beds and bedmaking, then baths and packs, local applications, with enemata, enteroclysis, etc. Then follows a chapter on the temperature, pulse, respiration and charts. Observation and examination, examination of vomitus, etc., bandages and splints, medicines, and poisons are the head-

ings of other chapters. Elementary bacteriology and theories of immunity are discussed in 50 pages. This is followed by eight chapters on surgical conditions. Symptoms and conditions frequently met with, three chapters on food, and one on the head nurse and ward management practically complete the book, except for a brief appendix on recipes, the index and introduction. There are numerous points to which exception might be taken, but they are not of vital importance and so can be passed over, without further notice except to draw attention to the fact that training of nurses varies largely in the different schools and that what are taught as the best methods of procedure in certain cases are not so considered by others. This remark is also applicable to what should or should not be taught nurses, and on this point also there is room for difference of opinion with Miss Sanders in some instances. None the less her book is one of the best that has appeared, for her instruction is reliable and serviceable.

The Surgical Clinics of John B. Murphy, M. D. Volume II. Number 1. (*Philadelphia and London: W. B. Saunders Company, February, 1913.*)

"Open Treatment of Fractures," "Fracture and Luxation of Neck of Humerus" and "Tuberculosis of the Knee: Arthrodesis" are some of the most noteworthy "Clinics" in this volume. They are well illustrated by X-ray and other photographs. The other "Clinics" are shorter and not so abundantly illustrated, and yet while all will be valued by the author's followers, we cannot but question the importance of the publication of some of them.

Diseases of the Skin. By WILMOTT EVANS, M. D., B. Sc., F. R. C. S. (*Univ. of London Press.*)

It is rather difficult to understand why the publishers felt that there was a need for a text-book of this character, in view of the overabundance of the supply now on the market.

The most successful works on diseases of the skin, are those that combine a short but clear description of the symptoms encountered, with numerous illustrations, from good photographs of well selected cases, which have lost but little in their reproduction.

In this book the text can be criticised favorably, but the illustrations leave much to be desired. They are too few, not well selected, and have reproduced poorly. With only 32 pictures, four are used to show only one type of syphilis, the ulceration. One of the illustrations of ichthyosis is not typical of that disease, and could more appropriately represent an eczema or pellagra. That of lupus certainly looks like a crusted eczema. It is also rather peculiar, in a text-book on skin diseases, to give photographs of plants which may cause a dermatitis, without showing the disease caused by them; yet two, of the 32 illustrations, are of the primrose and poison ivy, but dermatitis venenata is not represented.

It is to be hoped that the second edition will evince more care in this most important feature of a text-book on diseases of the skin.

Diseases of the Eyes. By C. DEVEREUX MARSHALL, F. R. C. S. (*London: University of London Press, 1912.*)

Very little need be said about this book. It is similar in every way to several other text-books which are practically syllabi of larger text-books. In the main, it is the opinion of the reviewer that abbreviated text-books are not of much value, and no exception would be made in favor of the present volume. No light is thrown on mooted subjects, and it is questionable whether some subjects are discussed with sufficient fullness to satisfy State Boards of Medical Examiners. Furthermore, some common, yet important, subjects are omitted, such as vernal catarrh, transient episcleritis (Fuch's hot eye), superficial punctate, keratitis, Parinaud's conjunctivitis, etc.

In a number of places the author, as if in a hurry to close the discussion, makes statements at variance with accepted facts. We note this when he states that "Vesicular keratitis seldom occurs except in degenerated eyes," and also, when, on the subject of Tobacco Amblyopia, the following is met with—"When above directions are carried out, the sight will be *entirely* restored." The "Eye Signs" of Tabes and exophthalmic goitre are not even mentioned in its pages, nor is the Calmette tuberculin reaction spoken of, so that even if examined from the standpoint of the student or general practitioner, for whose use the book is intended, as indicated in the preface, the present volume is inadequate.

B. B. BROWNE, JR.

Diseases of the Eye. A Manual for Students and Practitioners. By J. HERBERT PARSONS, F. R. C. S. Second Edition. $4. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

This is the second edition of this text-book. It should be found a fairly satisfactory book for the beginner in the study of eye diseases, for it covers the whole subject, including a short résumé of the anatomy and physiology. A too positive dogmatism is, at places noted in its pages, but the main points are covered with a fair degree of fullness and accuracy. For the clinical worker this book would have less value since the suggestions offered for the actual management of eye cases are rather vague and indefinite.

B. B. BROWNE, JR.

The Anatomic Histological Processes of Bright's Disease and Their Relation to the Functional Changes. By HORST OERTEL. Director of the Russell Sage Institute of Pathology, New York. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

The problems underlying nephritis are so complex and there is so much difference of opinion among the best workers as to the fundamental changes in the different forms of nephritis that such a piece of scholarly work as Oertel's is welcome and deserves serious consideration. It is an important addition to the immense literature of the subject, and one that other workers along similar lines cannot afford to overlook. We regret the use of the term "Bright's disease," however, for it is vague and all scientists do not use it with exactly the same signification—this criticism only applies to the title and not the body of the work, in which he discusses mainly degenerative and exudative nephritis. The work is finely illustrated and students will find it abundantly worth their while to read it with care.

Glycosuria and Allied Conditions. By P. J. CAMMIDGE, M. D. $4.50. (*London and New York: Longmans, Green & Co., 1913.*)

The appearance of such a book at a time when our views of carbohydrate metabolism are in such a chaotic state, is most apt. These are the days of close co-operation between the diagnostician, internist and laboratory worker: mistakes, hasty conclusions, and consequent errors in judgment made by one, become harmfully effective through the others. Perhaps no commoner error is made than that which assumes any urinary reduction as due to glucose: and the individual thus doomed to the diabetic verdict becomes further the victim of some rule of thumb treatment, in no way in keeping with his metabolic conditions. The author has tried in this volume of 450 pages to make such errors impossible.

After a short chapter dealing in a general way with the properties and physiology of carbohydrates, there follows an exhaustive

and practical discussion of the detection and estimation of sugars occurring in the urine and blood, as well as of the so-called "acetone bodies," total nitrogen and ammonia: the section is specific as to the relative merits and fallacies of the tests, and includes a discussion of substances other than sugars which may cause reductions: the list could be further amplified.

The chapter on experimental glycosuria is a résumé of work done since the famous piqûre of Claude Bernard: proper emphasis is placed upon the close relationship now known to exist between the various ductless glands and the control of sugar metabolism: the observations of Lepine, Falta, Eppinger and Cushing are certainly stimulating, since they tend to show that "glycosuria is not a disease, but a symptom common to many pathological conditions."

Alimentary and transient glycosurias, their causes and diagnosis precede the 190 pages devoted to a detailed discussion of true diabetes mellitus, its urinary findings, clinical symptoms, complications of the disease, its pathological basis, and the methods at hand for its early recognition: the *raison d' être* of many common subjective complaints is excellently and tersely described.

Through a concise review of normal metabolism the author makes clear the altered conditions in diabetes and the all essential factor in successful treatment, namely, individual study: he gives in detail the methods used by him in determining the proper dietetic régime: they differ in no essential details from those of von Noorden, and are perhaps not as clear or easy of application: the rational of various drug and glandular therapies is reviewed in the light of our modern pharmacological knowledge. The concluding three chapters deal with the subjects of levulosuria, lactosuria, pentosuria, alkaptonuria, and diabetes insipidus, the book ending with an admirable appendix devoted to a more minute and chemical consideration of the reactions of carbohydrates and allied bodies.

The book is readable, viewed both from the author's style and printer's presentation of the matter: typographical errors, if present, are remarkably few: an appropriate bibliography is given at the end of each chapter, a method highly to be commended; the index alone can justly be criticised from the standpoint of efficiency. The reviewer unhesitatingly recommends the book to consultants, practitioners, and students, as the best work of its kind in the English language. S. R. M.

Malaria: Cause and Control. By William B. Herms, M. A. Illustrated. (*New York: The Macmillan Company, 1913.*)

This small book is the result of the author's work in attempting to rid California of mosquitoes and is an excellent guide for other communities pursuing the same task. Mr. Herms has probably had greater experience in the controling of malaria than any one else in the country and has written an admirable treatise. He covers all the essential points which need consideration, and has gathered a lot of material which is unusual but of distinct usefulness as showing how to go about the work. This book is really an important and valuable contribution, and we wish there were similar ones treating in an equally striking and appropriate manner some of our other common diseases—*ex.*, typhoid.

Ophthalmic Surgery. By Dr. Josef Meller, Vienna. Edited by Dr. William M. Sweet. Illustrated. Second Edition, Thoroughly Revised. $3.50. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

This is the second edition of this work. The author describes the operative procedures which have been adopted in the eye clinic of Professor Fuch of Vienna. Quite a considerable portion of the text is given to a description of lid operations, which, as a rule, every operator modifies, more or less, to suit himself and the particular case at hand. The description of the standard operations for cataract, glaucoma, and the enucleation of the eyeball, etc., are quite satisfactory. An abundance of well drawn pictures accompany the text. B. B. Browne, Jr.

Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India. (*Calcutta: Superintendent Government Printing, India, 1912.*)

No. 57. Studies on the Flagellates of the Genera Herpelomonas, Crithidia and Rhynchoidomonas. By Captain W. S. Patton, M. B., etc. Price 1/2.

No. 58 and 59. Studies on the Mouth Parts and Sucking Apparatus of the Blood-Sucking Diptera. By Captain F. W. Cragg, M. B., etc. Price 1/. and 1/11.

The subtitle of Captain Patton's paper is The Morphology and Life History of Herpelomonas Culicis,—Novy, MacNeal and Terry, and his study is therefore of special interest to a few students in America as the parasite found in India is probably identical with that found in this country. This memoir and the two by Captain Cragg are important as they help us to a more accurate knowledge of the ways in which diseases are transmitted. They are purely scientific and therefore will appeal to but a special class of workers to whose attention we are glad to call them.

The Hunterian Lectures on Colour-Vision and Colour-Blindness. By Professor F. W. Edridge-Green, F. R. C. S. (Eng.). $1.50. (*New York: Paul B. Hoeber, 1912.*)

The material in this work is somewhat old, being delivered in the form of lectures in February, 1911. The views are speculative, and the author's ideas may have changed by this time.

B. B. Browne, Jr.

Systematic Case-Taking. By Henry Lawrence McKisack, M. D. $1.50. (*New York: Paul B. Hoeber, 1913.*)

To internes or house-officers who have not been well instructed in writing histories of patients, the study of this small volume should prove most helpful. It is an excellent guide, compact and concise. The author has divided his matter into nine chapters: 1. Preliminary enquiries. 2. General examination. 3. The thorax. 4. Respiratory system. 5. Circulatory system. 6. Blood. 7. The abdomen. 8. Examination of the urine. 9. Nervous system. The fault with most case-taking is that no system is followed, and the history naturally becomes a jumble as the clinical clerk jumps from one organ to another, and there is no sequence in his development of the patient's history and condition. A student who makes a habit of taking his histories systematically will find it an immense help to him in all his work. It is an evidence of orderly thought and a well developed case history leads up far more precisely and accurately to the correct diagnosis than any other. Snap diagnoses may be correct, but they are the result of bad training and have an evil influence on the student's mind. This manual should serve an excellent end in teaching students how to go about their work, and in developing in them good methods of study. We commend it heartily.

Surgery: Its Principles and Practice. By Various Authors. Edited by W. W. Keen, M. D., etc. Volume VI. Illustrated. (*Philadelphia and London: W. B. Saunders Company, 1913.*)

Between 1906 and 1909 this surgery was published in five volumes. To bring it as nearly as possible up to date this supplementary volume has been added. With but very few exceptions the original authors have described the advances made in the special branch of surgery previously written on by them. Seventy chapters, of a little over 1000 pages altogether, covering the whole

field of surgery, have thus been contributed by 61 physicians. The longest chapter of nearly 100 pages is in the surgery of the female genito-urinary organs, and we question whether the advances made in this branch of surgery justify a chapter so much longer than any other. Important surgical developments since 1909 embrace the treatment of cancer by fulguration, new methods of anæsthesia, the use of salvarsan, the opening of the thorax, operations on the hypophysis, etc., all of which are noticed in this volume, which makes a valuable addition to the system, and both Dr. Keen and the publishers are to be congratulated on having so successfully completed the original undertaking. The profession will be grateful for this final volume which makes the surgery as nearly perfect as it can be. That the editor should have succeeded in getting all the original writers to contribute these additional chapters shows the warm interest they took in the work, and their justified feeling that the surgery was a success and heartily appreciated by American surgeons.

International Clinics. Twenty-third Series. Volume I. (*Philadelphia and London: J. B. Lippincott Company, 1913.*)

More than a hundred pages of this volume are given to an interesting review of the progress in medicine during the year 1912. The article has been carefully prepared by Drs. Cattell and Johnson. A couple of noteworthy clinics are by Rugh and Abham—the former reports ten cases of Pott's disease of the spine treated by Albee's method of bone grafting; and the latter some cases of aneurism much improved by concussion of the seventh cervical spine. There are several other papers which it will repay the student to read attentively.

The Principles and Practice of Obstetrics. By JOSEPH B. DE LEE, A. M., M. D. Illustrated. $8. (*Philadelphia and London: W. B. Saunders Co., 1913.*)

This ambitious text-book of more than a thousand pages is chiefly notable for the illustrations which, we are told, required "the tireless labor of three artists extending over a period of eight years." Most of the microscopic drawings by Miss Grace Amidon have been made from specimens; they are accurate and well done. Of the other illustrations a few are original, a few are taken from the author's text-book for nurses, but most of them have been redrawn from German works on obstetrics and embryology, especially from Bumm's *Grundriss zum Studium der Geburtshülfe.* Credit for these illustrations is not given at the place of insertion so frequently as is customary, though careful reading of the preface brings to light a frank acknowledgement of indebtedness. "To Bumm's matchless work," we read there, "the author is indebted for many ideas and for these, as well as for permission to copy some of his plates, the author is profoundly grateful." This statement, it seems to the reviewer, would be more accurate did it acknowledge indebtedness for *some* of the ideas and *many* of the plates.

Many of the ideas Dr. De Lee expresses are original. For example, in his introduction he declares that child-bearing is not a normal process. Such a gloomy view of reproduction would deserve severe criticism were not the book intended for physicians and medical students whose experience will demonstrate its incorrectness. Even in cases of contracted pelvis more than three-fourths of labors are normal. It is also novel to find in a text-book on obstetrics a discussion of the mental state of the unborn child—a discussion which leads to the conclusion that "a vague and obscure will intervenes in the production of these (fœtal) movements." As a matter of fact, there is no evidence to indicate that the fœtal brain functions; on the contrary we have reason to believe that the fœtus is a spinal animal and that its movements are entirely reflex. An infant born without a brain may live several days, which proves that a brain is not needed during fœtal development. For similar reasons we cannot accept the view that the uterine contractions during labor cause the fœtus pain.

We do not agree with the author in his opinion that he has been dogmatic in omitting polemics, but in another direction he has been very dogmatic. In the literature he selects for quotation he shows a strong bias. Thus, with regard to the problem of sex-determination, which has stimulated many biologists, to undertake investigations of fundamental importance, De Lee does not fairly summarize the facts as they are known to-day. So far as human beings are concerned the question remains unsettled, to be sure; but there is better reason to believe that sex is inherited from the spermatozöon than from the ovum. The opposite view is held by the author as he overlooks the observations of a number of investigators who found that in numerous animal species the spermatozöon is the vital factor in this problem. Similarly in describing fœtal nutrition no reference is made to Cohnstein and Zuntz whose experiments have revealed in a very complete fashion the laws according to which gases pass through the placenta. This is all the more important since our knowledge of the mechanism by which other substances pass the placenta is very imperfect and in great part theoretical.

Although the author's views regarding the unsettled problems in obstetrics are not always in accord with the highest authority, his description of the more practical side of the subject is reliable and up to date. The book is logically arranged except for the section on the hygiene of pregnancy which should rightly precede the chapters on labor and the lying-in period. Two-thirds of the book are comprised in the sections on the pathology of pregnancy, labor, and the puerperium. Puerperal infection is discussed extensively and detailed directions are given for the performance of obstetrical operations.

Nervous and Mental Monograph Series, No. 12. Cerebellar Functions. By DR. ANDRE-THOMAS. $3. (*New York: The Journal of Nervous and Mental Disease Publishing Co., 1912.*)

This is the most recent of the series of monographs published by the editors of *The Journal of Nervous and Mental Diseases.* The translation is good; and English readers, especially the otologists and neurologists, will find it highly entertaining and instructive reading. The author is an investigator of world-wide renown, and has made many contributions to the physiology of the cerebellar apparatus. It is to be regretted, however, that no mention is made of the clinical observations of Barony and the Vienna school.

The subject of cerebellar discords and their localization is but little understood at the present time, but great progress is now being made along this line. It is especially desirable, therefore, that those interested in neurology should acquaint themselves with this monograph, and, through its extensive bibliography, with the most important contributions to this subject.

S. J. CROWE.

Progressive Medicine. Edited by HOBART AMORY HARE, M. D., etc. Assisted by LEIGHTON F. APPLEMAN, M. D. Volume I, (*Philadelphia and New York: Lea & Febiger, March, 1913.*)

Any physician, who has not a knowledge of French or German, or the time to read widely, will keep himself well abreast of the times by the use of these quarterly volumes of *Progressive Medicine.* In this last one Frazier presents the newest information on the surgery of the head, neck, and thorax; Ruhräh on infectious diseases, including acute rheumatism, croupous pneumonia and influenza; Crandall on diseases of children; Wood on rhinology and laryngology, and Duel on otology. The articles are well prepared and interesting, and cover these different branches of medicine satisfactorily.

American Association for Study and Prevention of Infant Mortality. Transactions of the Third Annual Meeting, Cleveland, Ohio, 1912. (*Baltimore: The Franklin Printing Co., 1913.*)

The subjects especially discussed at this meeting were birth, registration, continuation schools, eugenics, progress in preventive work, mid-wifery, housing, and nursing and social work, all very important in the consideration of infant mortality. There are many interesting papers in this volume by Drs. Putnam, Holt, Helmholtz, Knox, Mr. Goddard, Miss Lathrop and others, and the transactions are a valuable source of information on a variety of topics relating to the welfare of infants. This new association is doing excellent work in a most fundamental line, and is becoming most helpful not only to physicians but to all social workers.

A Practical Text-Book of the Diseases of Women. By Arthur H. N. Lewers, M. D. Seventh Edition. $4. (*New York: Paul B. Holber, 1912.*)

This little volume belongs to an English Practical Series set, and possesses the general characteristics of this type of medical publication. It has long been well known and popular in the British Isles, and is evidently filling a place of usefulness, as is shown by the appearance of this seventh edition. The entire work has been revised and considerably enlarged, the chapters on cancer of the uterus and fibroid tumors particularly having been amplified in this revision. The orderly division of subject-matter, simplicity and conciseness of discussion, and the insertion of numerous illustrative cases adapt the book fairly well to the actual needs of the average medical student. It, however, must not be considered an exhaustive treatise on gynecology.

Pathology and Treatment of Diseases of Women. By A. Martin and Pii. Jung. English Translation of the Fourth German Edition. By Henry Schmitz, M. D. $5. (*New York: Rebman Co., 1912.*)

This English translation of one of the most authoritative, substantial and popular of the smaller German text-books on gynecology should be gratefully received by a large proportion of the American profession. The book is admirable in many respects. It is concise, judiciously comprehensive and logically arranged. The numerous illustrations are helpful in elucidating the text, but are poor from an artistic standpoint. The translation has been clumsily done—that is, it is too literal, so that one encounters numerous sentences in which both the choice and arrangement of words are bad. These, however, are minor faults that do not seriously detract from the worth of the book. The pathological side of gynecology is brought strikingly into the foreground, a fact which, when one considers the eminence and experience of the authors, makes conspicuously evident one of the deficiencies of many of the American text-books on this subject. On the whole, the book will prove profitable reading alike to student and teacher, practitioner and specialist. It can be unhesitatingly recommended. E. H. R.

Diseases of Women. By Thomas George Stevens, M. D., etc. (*London: University of London Press, 1912.*)

This little book can scarcely be considered as being more than a concise introduction to gynecology. As far as it goes, however, it is a creditable production, and is very readable. Certainly it will prove acceptable to those who desire only a superficial knowledge of this branch of medicine. The photomicrographs deserve special mention, inasmuch as they are far superior to those usually seen in manuals of this size. A perusal of the book leaves the impression that the author would be equal to a much more pretentious and valuable production.

Private Duty Nursing. By Katharine De Witt, R. N. $1.50. (*Philadelphia and London: J. B. Lippincott Company, 1913.*)

Miss De Witt has written a serviceable series of talks for nurses, which are now combined in neat book form. Many of them will be familiar to readers of the *American Journal of Nursing.* It is a rather sad commentary on the standards of nursing in this country that the authoress has to lay stress on points of etiquette. It would seem that common sense or the sense of propriety would prevent women making the mistakes they so often do. This is an excellent book for the ill-educated nurse, for Miss De Witt writes in a simple and effective way of what a private nurse should be, and of her responsibilities, and the advice given is helpful throughout. All the essential features of a nurse's relations with private patients are carefully considered, and she is shown clearly what she ought and ought not do.

BOOKS RECEIVED.

The Diseases of the Skin. By Willmott Evans, M. D., B. S., B. Sc., F. R. C. S. With thirty-two illustrations. [1912]. 8vo. 375 pages. University of London Press, London; Oxford University Press, New York.

The Medical Diseases of Children. By T. R. C. Whipham, M. A., M. D. (Oxon.), M. R. C. P. With sixty-seven illustrations. [1912]. 8vo. 417 pages. University of London Press, London; Oxford University Press, New York.

Minor Surgery. By Leonard A. Bidwell, F. R. C. S. Second edition revised and enlarged. With one hundred and twenty-nine illustrations. [1912]. 8vo. 299 pages. University of London Press, London; Oxford University Press, New York.

The Surgery of the Skull and Brain. By L. Bathe Rawling, F. R. C. S. 1912. 8vo. 340 pages. Henry Frowde, London; Hodder & Stoughton, London.

Health and Longevity Through Rational Diet. Practical Hints in Regard to Food and the Usefulness or Harmful Effects of the Various Articles of Diet. By Dr. Arnold Lorand. 1912. 8vo. 416 pages. F. A. Davis Company, Philadelphia.

The Labyrinth. An Aid to the Study of Inflammations of the Internal Ear. By Alfred Braun, M. D., and Isidore Friesner, M. D. With fifty figures in the text and thirty-four half tones on thirty-two plates. [1913]. 8vo. 250 pages. Rebman Company, New York.

Diet and Hygiene in Diseases of the Skin. By L. Duncan Bulkley, A. M., M. D. 1913. 8vo. 194 pages. Paul B. Hoeber, New York.

Report of the Pellagra Commission of the State of Illinois. November, 1911. 1912. 8vo. 250 pages. Illinois State Journal Co., Springfield.

Medical Men and the Law. A Modern Treatise on the Legal Rights, Duties and Liabilities of Physicians and Surgeons. By Hugh Emmett Culbertson. 1913. 8vo. 325 pages. Lea & Febiger, Philadelphia and New York.

The Principles and Practice of Obstetrics. By Joseph B. De Lee, A. M., M. D. With 913 illustrations, 150 of them in colors. 1913. 4to. 1060 pages. W. B. Saunders Company, Philadelphia and London.

Psychanalysis. Its Theories and Practical Application. By A. A. Brill, Ph. B., M. D. 1913. 8vo. 337 pages. W. B. Saunders Company, Philadelphia and London.

The Development of the Human Body. A Manual of Human Embryology. By J. Playfair McMurrich, A. M., Ph. D., LL. D. Fourth edition, revised and enlarged. With 285 illustrations, several of which are printed in colors. 1913. 12 mo. 495 pages. P. Blakiston's Son & Co., Philadelphia.

The Surgical Clinics of John B. Murphy, M. D. At Mercy Hospital, Chicago. December, 1912. Volume I. Number 6, 1912. 8vo. 931 pages. W. B. Saunders Company, Philadelphia and London.

Guy's Hospital Reports. Edited by F. J. Steward, M. S., and Herbert French, M. D. Vol. LXVI, being Vol. LI of the Third Series. 1912. 8vo. 412 pages. J. & A. Churchill, London.

Golden Rules of Surgery. By Augustus Charles Bernays, A. M., M. D., Hdlbg., M. C. R. S., Eng. Second edition, revised and rewritten. By William Thomas Coughlin, M. D. 1913. 12mo. 281 pages. C. V. Mosby Company, St. Louis.

Transactions of the American Gynecological Society. Volume 37. For the year 1912. 1912. 8vo. 502 pages. Wm. J. Dornan, Philadelphia.

A Reference Handbook of the Medical Sciences. Embracing the Entire Range of Scientific and Practical Medicine and Allied Science. By various writers. First and second editions edited by Albert H. Buck, M. D. Third edition completely revised and rewritten. Edited by Thomas Lathrop Stedman, A. M., M. D. Complete in eight volumes. Volume I illustrated by numerous chromolithographs and 611 fine half-tone and wood engravings. 1913. 4to. 928 pages. William Wood and Company, New York.

Transactions of the Royal Academy of Medicine in Ireland. Volume XXX. Edited by J. Alfred Scott, M. A., M. D., F. R. C. S. I. 1912. 8vo. 521 pages. John Falconer, Dublin.

Index-Catalogue of the Library of the Surgeon-General's Office, United States Army. Authors and Subjects. Second series. Volume XVII, Suaheli-Testut. 1912. 4to. 788 pages. Washington.

Handbook of Diseases of the Rectum. By Louis J. Hirschman, M. D. With one hundred and seventy-two illustrations, mostly original, including four colored plates. Second edition, revised and re-written. 1913. 8vo. 339 pages. C. V. Mosby Company, St. Louis.

The Practice of Urology. A Surgical Treatise on Genito-Urinary Diseases Including Syphilis. By Charles H. Chetwood, M. D., LL. D. Profusely illustrated. 1913. 8vo. 816 pages. William Wood & Company, New York.

The Prospective Mother. A Handbook for Women during Pregnancy. By J. Morris Slemons. 1912. 12mo. 343 pages. D. Appleton & Company, New York and London.

Diseases of the Heart and Aorta. By Arthur Douglass Hirschfelder, M. D. With an Introductory Note by Lewellys F. Barker, M. D., LL. D. 344 Illustrations by the Author. Second edition. 1913. 8vo. 738 pages. J. B. Lippincott Company, Philadelphia and London.

The Illness and Death of Napoleon Bonaparte. (A Medical Criticism.) By Arnold Chaplin, M. D. (Cantab.), F. R. C. P. With three illustrations. 1913. 12mo. 112 pages. Hirschfeld Brothers, London.

Chloride of Lime in Sanitation. By Albert H. Hooker. 1913. 8vo. John Wiley & Sons, New York; Chapman & Hall, London.

Malaria. Cause and Control. By William B. Herms, M. A. Illustrated. 1913. 8vo. 163 pages. The Macmillan Company, New York.

The Surgical Clinics of John B. Murphy, M. D. At Mercy Hospital, Chicago. February, 1913. Volume II, number 1. 8vo. 179 pages. W. B. Saunders Company, Philadelphia and London.

Proceedings of the Canal Zone Medical Association. Isthmian Canal Commission for the Half Year, April to September, 1911. Volume IV, Part I. [1911.] 8vo. 238 pages. I. C. C. Press, Quartermaster's Department, Mount Hope, Canal Zone.

Glycosuria and Allied Conditions. By P. J. Cammidge, M. D. (Lond.) 1913. 8vo. 467 pages. Longmans, Green & Co., New York; Edward Arnold, London.

Dreams and Myths. A Study in Race Psychology. By Dr. Karl Abraham. Translated by William A. White, M. D. Nervous and Mental Disease Monograph Series, No. 15. 1913. 8vo. 74 pages. The Journal of Nervous and Mental Disease Publishing Company, New York.

Pathology. A Manual for Teachers and Students. By W. T. Councilman, M. D. 1912. 8vo. 405 pages. W. M. Leonard, Boston.

Mind and Health. With an Examination of Some Systems of Divine Healing. By Edward E. Weaver, Ph. D. With an Introduction by G. Stanley Hall, Ph. D., LL. D. 1913. 12mo. 500 pages. The Macmillan Company, New York.

The Johns Hopkins University Circular. 1912. Volume XXXI. Whole Nos. 241-250. 1912. 8vo. The Johns Hopkins Press, Baltimore.

Organic and Functional Nervous Diseases. A Text-Book of Neurology. By M. Allen Starr, M. D., Ph. D., LL. D., Sc. D. Fourth edition, thoroughly revised. Illustrated wth 323 engravings in the text and 30 plates in colors and monochrome. 1913. 8vo. 970 pages. Lea & Febiger, New York and Philadelphia.

Progressive Medicine. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M. D. Assisted by Leighton F. Appleman, M. D. Volume I. March, 1913. 8vo. 361 pages. Lea & Febiger, Philadelphia and New York.

PROSPECTUS OF SUMMER COURSES FOR GRADUATES IN MEDICINE.

THE JOHNS HOPKINS UNIVERSITY—THE JOHNS HOPKINS HOSPITAL.

JUNE 2 TO JULY 15, 1913.

In co-operation with the Johns Hopkins Hospital, the following courses are offered to graduates in medicine. Instruction will begin on Monday, June 2d and end on Tuesday, July 15th.

The clinical courses are limited to graduates in medicine, but the courses in Physiology, Physiological Chemistry, Pharmacology and Therapeutics, and Bacteriology are also open to undergraduate students.

PHYSIOLOGY.

DR. C. D. SNYDER, Associate Professor of Physiology.

This course is intended to give the student an opportunity to become acquainted with some of the chief methods employed in teaching and in research.

Especial attention will be given to the mechanisms of circulation and respiration that can be demonstrated upon mammals, and to methods of recording and accurately measuring such phenomena as venous pulse and venous and arterial pressures in man.

Monday, Wednesday and Friday, 8 a. m. to 12 m.

PHYSIOLOGICAL CHEMISTRY.

DR. E. K. MARSHALL, JR., Assistant in Physiological Chemistry.

This course will consist of lectures covering the chemistry of the proteins, sugars, fats, blood, muscle, urine, ferments, etc., and of laboratory exercises in which the various tissues and fluids of the body will be studied.

Tuesday, Thursday and Saturday, 2 to 5 p. m.

PHARMACOLOGY AND THERAPEUTICS.

DR. L. G. ROWNTREE, Associate in Experimental Therapeutics.

This course will consist of bedside instruction in therapeutics, and of laboratory demonstrations of the action of certain drugs, together with lectures on specific chemotherapy.

Monday, Wednesday and Friday, 2 to 5 p. m.

BACTERIOLOGY.

DR. L. P. SHIPPEN, Instructor in Hygiene and Bacteriology.

This course will consist of practical laboratory exercises covering the preparation of culture media, the principles of sterilization and the methods of isolating, cultivating, and studying bacteria.

Tuesday, Thursday and Saturday, 10 a. m. to 1 p. m.

MEDICINE.

The following courses will be given:

I. **Practical Medicine**—DR. L. V. HAMMAN, and DR. F. J. SLADEN, Associates in Medicine.
A course in practical medicine consisting of ward rounds. Daily, 9 to 11 a. m.

II. **Clinical Microscopy**—DR. C. G. GUTHRIE, Instructor in Charge of the Clinical Laboratory.
The course consists of lectures and laboratory work, the material from the wards being utilized.
Monday, Wednesday and Friday, 2 to 4.30 p. m.

III. **Serum Diagnosis**—DR. P. W. CLOUGH, Instructor in Charge of the Biological Laboratory of the Medical Clinic, and DR. C. R. AUSTRIAN, Assistant in Charge of the Laboratory of the Phipps Dispensary.
The course consists of lectures and laboratory instruction covering the Wassermann reaction, Widal reaction, etc.
Tuesday, Thursday and Saturday, 2 to 4.30 p. m.

IV. **Diseases of the Circulation**—DR. A. D. HIRSCHFELDER, Associate in Charge of the Physiological Laboratory of the Medical Clinic, and DR. G. S. BOND, Assistant in Medicine.
The course covers the diagnosis and treatment of cardiac diseases, together with a study of blood-pressure, venous pulse, electrocardiograms, etc.
Tuesday, Thursday and Saturday, 2 to 4 p. m.

V. **Percussion and Auscultation**—DR. L. P. HAMBURGER, Associate in Medicine, and DR. S. WOLMAN, Instructor in Medicine.
Tuesday, Thursday and Saturday, 11 a. m. to 1 p. m.

VI. **Diseases of the Digestive Apparatus**—DR. T. R. BROWN, Associate in Medicine.
A course in the diseases of the digestive apparatus, with practical exercises in the use of the various diagnostic methods including sigmoidoscopy and fluoroscopy.
Monday, Wednesday and Friday, 11 a. m. to 12 m.

SURGERY.

The following courses will be given:

I. **Surgical Diagnosis**—DR. J. M. T. FINNEY, Professor of Clinical Surgery, assisted by DR. J. C. BLOODGOOD, Associate Professor of Surgery, DR. R. H. FOLLIS, Associate in Surgery, and DR. G. J. HEUER, Instructor in Surgery.
This course will consist of daily ward rounds and operating clinics.
Rounds: 9 a. m. to 10 a. m., and operations, 11 a. m. to 12 m.

II. **Surgical Pathology**—DR. W. E. DANDY, Assistant Resident Surgeon.
This course will consist of the gross and microscopic study of specimens from the surgical operating room.
Tuesday, Thursday and Saturday, 2 to 5 p. m.

III. **Operative Surgery on Animals**—DR. GEORGE WALKER, Associate in Surgery, assisted by DR. W. A. FISHER, Instructor in Surgery, and DR. R. D. MCCLURE, Assistant in Surgery.
In this course a limited number of students will perform a series of operations in abdominal, renal and blood-vessel surgery, under the immediate supervision of the instructors.
Monday, Wednesday and Friday, 2 to 5 p. m.

IV. **Genito-Urinary Surgery**—DR. J. T. GERAGHTY, Associate in Genito-Urinary Surgery, and DR. A. KEIDEL, Assistant Surgeon.
(a) Clinical instruction in history taking, routine genito-urinary examinations, urinary analysis, methods of microscopic examinations of secretions from the urethra, venereal sores (treponema pallida), prostate, etc., instrumental examination (including urethroscopy, but not cystoscopy), and methods of treatment.
Daily, 10 a. m. to 12 m.
(b) A course in cystoscopy and the diagnosis of renal conditions will be offered by Dr. Geraghty to a limited number of students who have had previous training in urology. This will consist of instruction in the methods and technique of cystoscopy, ureteral catheterization, and renal functional and differential diagnosis.
Tuesday, Thursday and Saturday, 12 to 1.30 p. m.

V. **Orthopedic Surgery**—DR. R. FAYERWEATHER, Assistant in Orthopedic Surgery.
Instruction in the methods of diagnosis and treatment, with particular attention to bone and joint tuberculosis and the various non-tuberculous joint affections.
Monday, Wednesday and Saturday, 10 to 12 m.
Instruction in the treatment of scoliosis will be given. Rounds will be made in the public wards one morning of each week.
Thursdays, 10 to 12 m.

VI. **Plastic Surgery**—DR. J. S. DAVIS, Instructor in Surgery.
In this course particular attention will be paid to wound healing, skin grafting, etc. Ward, dispensary and operative demonstrations will be given.
Monday, Wednesday and Friday, 10 to 12 m.

VII. **Rectal Surgery**—DR. H. B. STONE, Assistant Surgeon.
This course will include digital and protoscopic examinations, together with operations under general or local anesthesia.
Tuesday, Thursday and Saturday, 10 to 12 m.

VIII. **Radiography**—DR. F. H. BAETJER, Associate in Actinography, assisted by DR. C. A. WATERS.
Practical instruction in X-Ray laboratory. Daily, 10 to 12 m. Lecture on Saturday at noon.

IX. **Anesthesia**—DR. J. P. PRATT, Assistant Resident Surgeon.
Practical instruction in the administration of anesthetics in the operating room.
Tuesday, Thursday and Saturday, 10 to 12 m.

GYNECOLOGY.

The following courses will be given:

DRS. G. L. HUNNER, C. F. BURNAM and E. H. RICHARDSON, Associates in Gynecology, and DR. C. W. VEST, Resident Gynecologist.

I. **Operative Clinics**, preceded by pelvic examinations under anesthesia.
Daily, except Friday, 9 a. m. to 12 m.

II. **Ward-rounds**—Tuesdays and Thursdays, 9 to 10 a. m.

III. **Practical Work in the Dispensary**, including history taking, pelvic and abdominal examinations without anesthesia, and medical gynecology. Daily, 2 to 4 p. m.

IV. **Gynecological Pathology**—DR. ELIZABETH HURDON, Associate in Gynecology.
Gross and microscopic demonstration of specimens, and a special course in the examination of material removed by curettage.
Monday, Wednesday and Friday, 12 to 1 p. m.

V. **Cystoscopy**—DR. G. L. HUNNER.
Practical demonstrations in the cystoscopic clinic.
Tuesday, Thursday and Saturday, 2 to 4.30 p. m.

PEDIATRICS.

DR. JOHN HOWLAND, Professor of Pediatrics, and DR. E. A. PARK, Instructor in Pediatrics.

The course will consist of clinics and demonstrations of patients illustrating the more common diseases of infancy and childhood, especial emphasis being laid upon the methods of treatment of the nutritional diseases of infancy.

Monday, Wednesday and Friday, 11 a. m. to 1 p. m.

FEES.

A full day's work for the entire period in as many courses as can be taken without conflict in hours—$100. If Animal Surgery is taken, an additional charge of $25.00 will be made.

The fee for any one of the following courses is $25.00:

Physiology,	Orthopedic Surgery,
Physiological Chemistry,	Plastic Surgery,
Therapeutics,	Rectal Surgery,
Bacteriology,	Anesthesia,
Clinical Microscopy,	Gynecological Pathology.
Serum Diagnosis,	Gynecological Cystoscopy.
Diseases of Circulation,	Gynecological Dispensary,
Digestive Diseases,	Pediatrics.
Percussion and Auscultation,	

The fee for any one of the following courses is $50.00:

Medical Ward Rounds,	Surgical Diagnosis with Ward Rounds.
Radiography,	Genito-Urinary Surgery (a),
Gynecological Operative Course with Ward Rounds,	Genito-Urinary Surgery (b).
Surgical Operations,	

For Animal Surgery alone the fee is $75.00.

Persons desiring to take any of these courses must register at the Dean's Office, where they will receive the necessary credentials.

Courses cannot be changed after registration, except upon the payment of an additional fee.

In view of the fact that only a limited number can be admitted to some of the courses, it is advisable that applications be made in advance. Address the Dean of the Johns Hopkins Medical School, Baltimore.

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